IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE: ARMODAFINIL PATENT LITIGATION	MDL Docket No.: 1:10-md-2200-GMS
CEPHALON, INC. and CEPHALON FRANCE, Plaintiffs, v. WATSON LABORATORIES, INC., Defendant.	Civil Action No. 1:10-cv-00007-GMS
CEPHALON INC. and CEPHALON FRANCE, Plaintiffs, v. SANDOZ INC., Defendant.	Civil Action No. 1:10-cv-55-GMS Civil Action No. 1:11-cv-782-GMS
CEPHALON INC. and CEPHALON FRANCE, Plaintiffs, v. LUPIN LIMITED, Defendant.	Civil Action No. 1:10-cv-210-GMS
CEPHALON INC. and CEPHALON FRANCE, Plaintiffs, v. APOTEX INC., Defendant.	Civil Action No. 1:10-cv-695-GMS Civil Action No. 1:10-cv-1078-GMS

PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW
BY WATSON LABORATORIES, INC., SANDOZ INC.,
LUPIN LIMITED, AND APOTEX INC.

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DEFENDANTS' WITNESSES

Dr. Hollingsworth is an associate professor at Kansas State University. Tr. at 62:14-15 (Hollingsworth). Dr. Hollingsworth received a Ph.D. in organic chemistry in 1986 from Yale University. Tr. at 62:25-63:3 (Hollingsworth). He was a postdoctoral fellow and research assistant at Cambridge University, where he received a National Science Foundation NATO postdoctoral fellowship, which is awarded to approximately 50 scientists in the United States each year. Tr. at 63:17-21 (Hollingsworth).

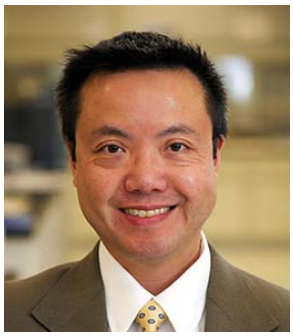
Dr. Hollingsworth has worked in the area of solid-state organic chemistry since 1979. Since becoming a faculty member, he has worked extensively in the fields of X-ray crystallography and spectroscopy for organic crystals. Tr. at 64:17-65:2 (Hollingsworth). Dr. Hollingsworth's extensive experience in organic synthesis and powder X-ray diffraction ("PXRD") is highly relevant to the issues in this case. Tr. at 65:6-9, 12-16 (Hollingsworth).

Dr. Hollingsworth was qualified as an expert in crystal engineering, X-ray diffraction, crystallography, organic chemical syntheses, organic solids, and polymorphism. Tr. at 66:4-10 (Hollingsworth).

Dr. Cima has been a professor at MIT for 25 years and is admitted to the National Academy of Engineering. Tr. at 371:14-20, 376:17-19 (Cima). Dr. Cima has extensive experience in the pharmaceutical industry; he has consulted for most of the major pharmaceutical companies, founded a number of pharmaceutical companies and has been involved in the development of numerous pharmaceutical compounds. Tr. at 372:16-18, 373:10-18, 376:16-377:3 (Cima).

Dr. Cima has extensive experience with the discovery and development of polymorphs and other solid forms of drug compounds, including conducting thousands of recrystallizations to obtain and purify crystalline drug products and conducting thousands of polymorphic screens to identify various solid forms of drug products. Tr. at 373:10-374:23, 375:2-13 (Cima). Dr. Cima is also an expert in PXRD and has conducted and analyzed thousands of PXRD measurements. Tr. at 375:25-376:5, 379:22-380:3 (Cima).

Dr. Cima was qualified as an expert in crystallization, polymorphism, and polymorph screening, and is the only witness qualified as an expert in pharmaceutical development in this case. Tr. at 379:22-380:3 (Cima).



Dr. Lee received his Ph.D. in organic chemistry in 1994, and has had about 18 years experience working as a synthetic organic or medicinal chemist. Tr. at 274:8-14, 275:11-14 (Lee); JTX-117. Dr. Lee is a co-author or co-inventor on eight peer-reviewed articles, 11 patents, and two pending patent applications. Tr. at 275:15-23 (Lee).

The Court accepted Dr. Lee as an expert in the fields of synthetic organic chemistry and medicinal chemistry. Tr. at 276:20-277:1 (Lee).

Dr. Robie received his Ph.D. in analytical chemistry from Rennselaer Polytechnic Institute in 1982. Tr. at 347:2-6 (Robie); JTX-119.2. He has authored or co-authored 20 peer-reviewed publications mostly relating to X-ray diffraction. Tr. at 348:14-20 (Robie). Dr. Robie has more than 30 years of experience characterizing materials using X-ray diffraction, including powder X-ray diffraction. Tr. at 348:9-13 (Robie). He performs PXRD analysis on about 15 to 20 sample materials in an average week. During his career, Dr. Robie has performed PXRD analysis on thousands of samples. Tr. at 346:22-347:1 (Robie).

The Court accepted Dr. Robie as a qualified expert in characterizing materials using PXRD. Tr. at 348:24-349:4 (Robie).

INTRODUCTION

The '570 patent-in-suit is one of a series of patents Cephalon has used to unlawfully extend its 30-plus year monopoly on the wakefulness drug compounds modafinil and armodafinil. The alleged invention of the '570 patent, however, is not inventive in any way. Its claims recite nothing more than what was taught in the prior art—a particular crystalline form of armodafinil and pharmaceutical compositions that use it. The predecessor compound modafinil was first patented by Cephalon in 1979. Armodafinil, the individual enantiomer, was subsequently described and claimed in Cephalon's prior art '855 patent, which issued in 1990. The crystalline form of armodafinil disclosed in the '855 patent is the ***same*** Form I crystalline armodafinil set forth in the asserted claims, which recite nothing more than a pharmaceutical composition consisting essentially of that form.

Defendants proved by clear and convincing evidence that the synthesis of armodafinil disclosed in the '855 patent results in polymorphic Form I. Their experts performed multiple replications of the technique for synthesizing armodafinil specifically described in the '855 patent. The result of each and every one of those experiments was Form I armodafinil. The remainder of the '855 patent teaches a person of ordinary skill that a pharmaceutical composition consisting essentially of Form I armodafinil would be an efficacious drug. The asserted claims cover nothing more than what the '855 patent expressly and inherently discloses, and are therefore invalid as anticipated.

Even assuming *arguendo* that the synthesis in the '855 patent did not produce Form I armodafinil, the asserted claims would still be invalid because obtaining and using that crystalline form in a pharmaceutical composition would have been obvious. Form I is undisputedly the most stable polymorphic form of armodafinil known. Accordingly, a person of ordinary skill in the art would have been motivated to use and obtain this form—with all of its

claimed properties—through no more than routine experimentation. Once crystalline armodafinil had been isolated, the '855 patent and the knowledge of a person of ordinary skill in the art at the time of the invention provided all the motivation and information needed to make a pharmaceutical composition consisting essentially of Form I armodafinil. The asserted claims are thus invalid as obvious over the prior art.

Accordingly, this Court should find the asserted claims invalid as anticipated and/or obvious, thus ending Cephalon's efforts to extend for another decade a pharmaceutical composition first disclosed and patented decades ago.

PROPOSED FINDINGS OF FACT

I. Factual and Technology Background

A. Cephalon's Wakefulness Patent Portfolio Dates Back 33 Years

1. This is a Hatch-Waxman lawsuit concerning Defendants' proposed generic armodafinil. Cephalon's NUVIGIL product allegedly contains Form I armodafinil as the active ingredient, and is used to increase wakefulness in certain patients including those with narcolepsy, sleep apnea, or shift work disorder. Tr. at 635:4-9 (Mallamo).

2. Armodafinil has a long history. In 1979, Cephalon's predecessor in France found a new molecule called "modafinil" and obtained U.S. Patent No. 4,177,290 ("the '290 patent") to cover it. Tr. at 84:21-25 (Hollingsworth); JTX-90.1-6. The '290 patent expired in 1998. Modafinil is the active ingredient in Cephalon's PROVIGIL drug, which has indications similar to those of NUVIGIL, and which has been sold commercially in the U.S. since 1998. Tr. at 647:2 (Mallamo); JTX-84.2; PTX-4.2.

3. Knowing that its modafinil patent would not last forever, Cephalon sought multiple and erroneous patent evergreening techniques to extend its PROVIGIL / NUVIGIL monopoly. For instance, it obtained U.S. Patent No. RE37,516, which covers uses of modafinil

of a defined particle size. This patent was recently found to be invalid and unenforceable. *Apotex Inc. v. Cephalon Inc.*, No. 06-2768, 2011 WL 6090696, at *28 (E.D. Pa. Nov. 7, 2011).

4. Another way Cephalon sought to extend its patent protection was to claim certain aspects of the "racemic" nature of modafinil's chemical structure. Tr. at 69:9-12 (Hollingsworth). A racemic compound has two components called "enantiomers." *See id.* Enantiomers have all of the same chemical components as each other, but with different spatial orientations. Tr. at 67:7-15 (Hollingsworth). They are non-superimposable mirror images of each other, often described with the analogy of right and left hands. Tr. at 412:18-21 (Cima).

5. Armodafinil is one of the enantiomers that makes up the racemic modafinil covered by the prior art '290 patent. *See* Tr. at 66:9-12 (Hollingsworth). In the 1980s—based on the teachings of the '290 patent—Cephalon's scientists undertook the straightforward task of synthesizing armodafinil separately from modafinil. Their work resulted in U.S. Patent No. 4,927,855 ("the '855 patent"), which claims, among other things, pharmaceutical compositions "consisting essentially of" armodafinil to use as an arousing agent and a stimulant. JTX-103.5, col 8, ll. 26-29. The '855 patent issued on May 22, 1990. JTX-103.1. It therefore qualifies as prior art to the '570 patent-in-suit under 35 U.S.C. § 102(b). *Id.;* JTX-1.2. Thus, it has long been known that armodafinil, just like modafinil, can be used as a pharmaceutical to promote wakefulness in humans. Tr. at 66:16-19 (Hollingsworth).

B. Cephalon's '570 Patent Discloses No New Technology

6. U.S. Patent No. 7,132,570 ("the '570 patent") was filed in the U.S. on December 18, 2003. JTX-1.2. The asserted claims 6 and 9 are directed to a pharmaceutical composition consisting essentially of a specific crystalline form of armodafinil called "Form I." JTX-1.38, col. 40, ll. 34-36, 40-41. The crystalline aspect of armodafinil simply refers to the fact that it is a solid in which individual molecules are arranged in a regularly repeating three-dimensional

pattern with long range order. Tr. at 68:10-23 (Hollingsworth).

7. To understand what it means to refer to "Form I" armodafinil, it is useful to understand that many molecules exist in different crystal forms called polymorphs. Tr. at 69:9-12 (Hollingsworth). Each polymorph has a unique crystal structure and characteristic "unit cell" that differs from other polymorphs. Tr. at 69:9-18 (Hollingsworth). In the pharmaceutical industry, polymorphs are typically named based on their order of appearance in the laboratory. Tr. at 70:18-23 (Hollingsworth), 389:5-9 (Cima). Thus, "Form I" (or "Form A") indicates the very first armodafinil polymorph identified. Tr. at 71:1-2 (Hollingsworth).

8. Scientists are able to distinguish between different polymorphs using a technique called powder X-ray diffraction ("PXRD"), which has been a routine analytical method as early as 1987. Tr. at 71:5-7 (Hollingsworth), 605:23-607:22 (Bernstein); DTX-32.34. In PXRD, X-rays are directed to a powdered sample and diffracted in a particular pattern unique to the polymorph in the sample. *E.g.,* Tr. at 71:11-18 (Hollingsworth). That pattern can be considered the "fingerprint" of the polymorph. *Id*.

9. The PXRD characteristics of a given crystalline material are reported in the form of a peak table and accompanying diffractogram. Tr. at 72:7-8 (Hollingsworth). The table identifies the spatial relationship of peaks (measured in "degrees 2-theta" or "2-θ") and their intensity or height. Tr. at 72:10-17 (Hollingsworth). That data is then graphically represented in the diffractogram, which charts the location of the peak along the horizontal x-axis, and intensity along the vertical y-axis. *Id*. The table also reports another measurement called "interplanar spacings" (sometimes called "d-spacings"). Tr. at 72:20-25 (Hollingsworth). Interplanar spacings are directly related to 2-theta values, and the two measures can easily be converted using a mathematical equation called Bragg's law. Tr. at 73:1-4, 20-23 (Hollingsworth). The 2-

theta and d-spacing values are intrinsic properties of the crystal. Tr. 73:9-12 (Hollingsworth); *see also*, Tr. at 382:12-18, 388:22-24, 421:21-25 (Cima).

C. Crystalline Armodafinil Was Well Known In The Prior Art

10. Much was known about the crystalline characteristics of armodafinil and its therapeutic uses before the '570 patent was filed. In fact, the inventors of the '570 patent initially swore to the PTO that armodafinil prepared according to the recrystallization conditions described in the '290 patent results in polymorphic Form I—just as is recited by the asserted claims. Tr. at 88:21-22, 89:10-16 (Hollingsworth); JTX-1.19 col. 2, ll. 42-47.

11. The prior art '855 patent includes detailed and extensive disclosures concerning crystalline armodafinil. It describes the preparation, synthesis and purification of armodafinil in a process called "Preparation I." JTX-103.3 col. 3, ll. 5-56. The '855 patent also reports on armodafinil's bioavailability, toxicity and therapeutic efficacy. JTX-103.1-.5 at abstract, col. 1 ll. 61-col. 2 ll. 9, col. 4 ll. 28-32, col. 6 ll. 34-36, 45-67, claims 2-6. As Cephalon admitted during prosecution of the '570 patent (PTX-118.7), the '855 patent teaches that Preparation I results in armodafinil (referred to internally at Cephalon as CRL 40982) "in the form of white ***crystals*** which are soluble in alcohols and acetone and insoluble in water and ether." Tr. at 103:3-6 (Hollingsworth), 381:10-12 (Cima); JTX-103.3, col. 3, ll. 52-54. Thus, the '855 patent expressly discloses that armodafinil can be a crystalline solid, just as is claimed in the '570 patent. Tr. at 391:12-18 (Cima).

12. The '855 patent further describes using the armodafinil that results from Preparation I—CRL 40982—in a pharmaceutical composition that may be administered once or twice a day in the form of tablets or capsules. Tr. at 148:4-13 (Hollingsworth), 429:23-430:3, 460:1-4 (Cima), 675:11-14, 20-21, 675:23-676:9 (Mallamo); JTX-103.4 col. 6, ll. 44-49. It also discloses that armodafinil was effective in human clinical trials, and has reasonable toxicity and

better bioavailability than modafinil. JTX-103.4 col. 5, ll. 28-32, col. 6, ll. 33-39, 45-57.

13. Claim 5 of the prior art '855 patent covers the use of armodafinil in combination with a physiologically acceptable excipient in a therapeutic composition comprising an amount effective as a central nervous system stimulant. Tr. at 150:2-4, 17-22 (Hollingsworth); JTX-103.5 col. 8, ll. 22-25. Claim 6 covers a pharmaceutical composition ***consisting essentially of*** armodafinil in combination with a physiologically acceptable medium for use in therapy as a central nervous system stimulant. Tr. at 150:11-16, 19-21 (Hollingsworth), 387:23-25, 429:23-430:3 (Cima); JTX-103.5 col. 8, ll. 26-29; *see also* Tr. at 677:17-20 (Mallamo).

14. The '855 patent, which expired in 2008, was listed in the FDA's Orange Book for NUVIGIL. JTX-131.4. Cephalon represented to the FDA that the '855 patent did ***not*** claim "a drug substance that is ***a different polymorph***. . ." from the Form I armodafinil that is covered by the '570 patent. JTX-132.1-3; Tr. at 681:12-17, 681:21-682:24, 683:3-5 (Mallamo). In other words, Cephalon ***admitted*** that ***both*** the asserted '570 patent and the prior art '855 patent cover Form I armodafinil. *Id.*

II. Armodafinil Form I Is the Natural and Inevitable Result of Performing Preparation I of Cephalon's Prior Art '855 Patent

15. The asserted claims add nothing inventive or patentable to the disclosures in the prior art. As compared to claim 6 of the '855 patent, the asserted claims recite only the interplanar spacings and 2-theta values intrinsic to Form I armodafinil.

16. Thus, the only question remaining at trial regarding anticipation was: which polymorphic form of armodafinil inherently results from performing Preparation I of the '855 patent? The evidence Defendants presented answered that question unequivocally and without a single contradictory result from Cephalon's experts: a person of ordinary skill in the art (a

"POSA")[1] will necessarily and inevitably obtain Form I armodafinil from following the prior art Preparation I process.

A. Dr. Hollingsworth's Experiments Show That Practicing Preparation I Results in Form I Armodafinil

17. At trial, Defendants' expert Dr. Hollingsworth presented insurmountable evidence that Form I armodafinil is the natural result flowing from Preparation I. He answered the question "What results from Preparation I?" in the most direct way possible: he carried it out, just as a POSA would have done in the late 1990s or early 2000s. Tr. at 123:17-21 (Hollingsworth). He completed two reproductions of Preparation I, and many additional recrystallizations from ethanol, as set out in the '855 patent. Tr. at 91:2-4 (Hollingsworth), 773:5-7 (Myerson).

18. Then, to determine the polymorphic form of the armodafinil he synthesized pursuant to Preparation I of the '855 patent, Dr. Hollingsworth used PXRD analysis—a technique universally recognized as the "gold standard" for determining polymorphic forms. Tr. at 82:5-9, 106:6-7 (Hollingsworth). His PXRD analyses confirmed that his experiments produced Form I armodafinil each and every time. Tr. at 91:9-10 (Hollingsworth).

B. Dr. Hollingsworth Practiced Preparation I as a POSA Would Have Done and Obtained Form I Armodafinil Each and Every Time

19. Preparation I describes a four-step procedure for the synthesis and purification of Form I armodafinil. Tr. at 95:4-6 (Hollingsworth), 717:18-20 (Myerson); JTX-103.3 col. 3, ll. 5-

[1] While the parties' experts offered different views as to the definition of a POSA, Defendants' experts agreed that their opinions were not dependant on which definition the Court adopted. Defendants' experts provided specific testimony regarding that skill level (*see* Tr. at 87:3-18 (Hollingsworth), 384:17-385:5 (Cima)), but their opinions in this matter would remain unchanged if the Court agrees with Cephalon's experts about the definition of a POSA. *See, e.g.,* Tr. at 86:23-88:1 (Hollingsworth); 384:17-385:23 (Cima); 545:23-546:11 (Bernstein).

57. The chemistry involved is straightforward, clean, and uncomplicated. Tr. at 279:9-17 (Lee). Dr. Hollingsworth performed each of the four steps at least twice, and it is undisputed that he did so as a POSA would have done. Tr. at 95:4-6, 96:23-25, 98:24-25, 100:17-101:2, 103:6-7, 123:17-21 (Hollingsworth), 717:18-20 (Myerson).

20. The purpose of step (a) in the overall synthesis is to separate the two enantiomers of modafilic acid by reacting the enantiomers with a complexing agent. Tr. at 95:24-96:5 (Hollingsworth). Dr. Hollingsworth performed step (a)—exactly as it would have been understood and performed by a POSA in the late 1990s or early 2000s—four times. Tr. at 97:1-21 (Hollingsworth); JTX-39.13 *et seq.*, .27 *et seq.*, .43 *et seq.*, .93 *et seq*.

21. The purpose of step (b) is to liberate the R-modafilic acid from the complex created in step (a). Tr. at 100:3-9 (Hollingsworth). Dr. Hollingsworth also performed step (b)—exactly as it would have been understood and performed by a POSA in the late 1990s or early 2000s—four times. Tr. at 98:24-25, 99:6-7 (Hollingsworth); JTX-39.31 *et seq.*, .59 *et seq.*, .85 *et seq.*; JTX-40.35 *et seq*.

22. Step (c) of Preparation I provides for the conversion of the product of step (b) into its methyl ester. Tr. at 110:4-10 (Hollingsworth). Dr. Hollingsworth performed step (c) twice and, like steps (a) and (b), he replicated it as it would have been understood and performed by a POSA. Tr. at 100:17-101:2, 101:14-16 (Hollingsworth); JTX-39.77 *et seq*.; JTX-40.77 *et seq*.

23. The purpose of step (d) of Preparation I is to convert the methyl ester into armodafinil and to purify the resulting armodafinil. Tr. at 101:21-102:1 (Hollingsworth). The last part of step (d) calls for the material to be "recrystallized from ethanol." Tr. at 102:12-14 (Hollingsworth); JTX-103.3, col. 3, ll. 50. Dr. Hollingsworth performed step (d) twice in a manner consistent with the teachings of the '855 patent. Tr. at 103:7; 106:1-2 (Hollingsworth);

INTRODUCTION

The '570 patent-in-suit is one of a series of patents Cephalon has used to unlawfully extend its 30-plus year monopoly on the wakefulness drug compounds modafinil and armodafinil. The alleged invention of the '570 patent, however, is not inventive in any way. Its claims recite nothing more than what was taught in the prior art—a particular crystalline form of armodafinil and pharmaceutical compositions that use it. The predecessor compound modafinil was first patented by Cephalon in 1979. Armodafinil, the individual enantiomer, was subsequently described and claimed in Cephalon's prior art '855 patent, which issued in 1990. The crystalline form of armodafinil disclosed in the '855 patent is the ***same*** Form I crystalline armodafinil set forth in the asserted claims, which recite nothing more than a pharmaceutical composition consisting essentially of that form.

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2. Armodafinil has a long history. In 1979, Cephalon's predecessor in France found a new molecule called "modafinil" and obtained U.S. Patent No. 4,177,290 ("the '290 patent") to cover it. Tr. at 84:21-25 (Hollingsworth); JTX-90.1-6. The '290 patent expired in 1998. Modafinil is the active ingredient in Cephalon's PROVIGIL drug, which has indications similar to those of NUVIGIL, and which has been sold commercially in the U.S. since 1998. Tr. at 647:2 (Mallamo); JTX-84.2; PTX-4.2.

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5. Armodafinil is one of the enantiomers that makes up the racemic modafinil covered by the prior art '290 patent. *See* Tr. at 66:9-12 (Hollingsworth). In the 1980s—based on the teachings of the '290 patent—Cephalon's scientists undertook the straightforward task of synthesizing armodafinil separately from modafinil. Their work resulted in U.S. Patent No. 4,927,855 ("the '855 patent"), which claims, among other things, pharmaceutical compositions "consisting essentially of" armodafinil to use as an arousing agent and a stimulant. JTX-103.5, col 8, ll. 26-29. The '855 patent issued on May 22, 1990. JTX-103.1. It therefore qualifies as prior art to the '570 patent-in-suit under 35 U.S.C. § 102(b). *Id.;* JTX-1.2. Thus, it has long been known that armodafinil, just like modafinil, can be used as a pharmaceutical to promote wakefulness in humans. Tr. at 66:16-19 (Hollingsworth).

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6. U.S. Patent No. 7,132,570 ("the '570 patent") was filed in the U.S. on December 18, 2003. JTX-1.2. The asserted claims 6 and 9 are directed to a pharmaceutical composition consisting essentially of a specific crystalline form of armodafinil called "Form I." JTX-1.38, col. 40, ll. 34-36, 40-41. The crystalline aspect of armodafinil simply refers to the fact that it is a solid in which individual molecules are arranged in a regularly repeating three-dimensional

pattern with long range order. Tr. at 68:10-23 (Hollingsworth).

7. To understand what it means to refer to "Form I" armodafinil, it is useful to understand that many molecules exist in different crystal forms called polymorphs. Tr. at 69:9-12 (Hollingsworth). Each polymorph has a unique crystal structure and characteristic "unit cell" that differs from other polymorphs. Tr. at 69:9-18 (Hollingsworth). In the pharmaceutical industry, polymorphs are typically named based on their order of appearance in the laboratory. Tr. at 70:18-23 (Hollingsworth), 389:5-9 (Cima). Thus, "Form I" (or "Form A") indicates the very first armodafinil polymorph identified. Tr. at 71:1-2 (Hollingsworth).

8. Scientists are able to distinguish between different polymorphs using a technique called powder X-ray diffraction ("PXRD"), which has been a routine analytical method as early as 1987. Tr. at 71:5-7 (Hollingsworth), 605:23-607:22 (Bernstein); DTX-32.34. In PXRD, X-rays are directed to a powdered sample and diffracted in a particular pattern unique to the polymorph in the sample. *E.g.,* Tr. at 71:11-18 (Hollingsworth). That pattern can be considered the "fingerprint" of the polymorph. *Id.*

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C. Crystalline Armodafinil Was Well Known In The Prior Art

10. Much was known about the crystalline characteristics of armodafinil and its therapeutic uses before the '570 patent was filed. In fact, the inventors of the '570 patent initially swore to the PTO that armodafinil prepared according to the recrystallization conditions described in the '290 patent results in polymorphic Form I—just as is recited by the asserted claims. Tr. at 88:21-22, 89:10-16 (Hollingsworth); JTX-1.19 col. 2, ll. 42-47.

11. The prior art '855 patent includes detailed and extensive disclosures concerning crystalline armodafinil. It describes the preparation, synthesis and purification of armodafinil in a process called "Preparation I." JTX-103.3 col. 3, ll. 5-56. The '855 patent also reports on armodafinil's bioavailability, toxicity and therapeutic efficacy. JTX-103.1-.5 at abstract, col. 1 ll. 61-col. 2 ll. 9, col. 4 ll. 28-32, col. 6 ll. 34-36, 45-67, claims 2-6. As Cephalon admitted during prosecution of the '570 patent (PTX-118.7), the '855 patent teaches that Preparation I results in armodafinil (referred to internally at Cephalon as CRL 40982) "in the form of white ***crystals*** which are soluble in alcohols and acetone and insoluble in water and ether." Tr. at 103:3-6 (Hollingsworth), 381:10-12 (Cima); JTX-103.3, col. 3, ll. 52-54. Thus, the '855 patent expressly discloses that armodafinil can be a crystalline solid, just as is claimed in the '570 patent. Tr. at 391:12-18 (Cima).

12. The '855 patent further describes using the armodafinil that results from Preparation I—CRL 40982—in a pharmaceutical composition that may be administered once or twice a day in the form of tablets or capsules. Tr. at 148:4-13 (Hollingsworth), 429:23-430:3, 460:1-4 (Cima), 675:11-14, 20-21, 675:23-676:9 (Mallamo); JTX-103.4 col. 6, ll. 44-49. It also discloses that armodafinil was effective in human clinical trials, and has reasonable toxicity and

better bioavailability than modafinil. JTX-103.4 col. 5, ll. 28-32, col. 6, ll. 33-39, 45-57.

13. Claim 5 of the prior art '855 patent covers the use of armodafinil in combination with a physiologically acceptable excipient in a therapeutic composition comprising an amount effective as a central nervous system stimulant. Tr. at 150:2-4, 17-22 (Hollingsworth); JTX-103.5 col. 8, ll. 22-25. Claim 6 covers a pharmaceutical composition ***consisting essentially of*** armodafinil in combination with a physiologically acceptable medium for use in therapy as a central nervous system stimulant. Tr. at 150:11-16, 19-21 (Hollingsworth), 387:23-25, 429:23-430:3 (Cima); JTX-103.5 col. 8, ll. 26-29; *see also* Tr. at 677:17-20 (Mallamo).

14. The '855 patent, which expired in 2008, was listed in the FDA's Orange Book for NUVIGIL. JTX-131.4. Cephalon represented to the FDA that the '855 patent did ***not*** claim "a drug substance that is ***a different polymorph***. . ." from the Form I armodafinil that is covered by the '570 patent. JTX-132.1-3; Tr. at 681:12-17, 681:21-682:24, 683:3-5 (Mallamo). In other words, Cephalon ***admitted*** that ***both*** the asserted '570 patent and the prior art '855 patent cover Form I armodafinil. *Id.*

II. Armodafinil Form I Is the Natural and Inevitable Result of Performing Preparation I of Cephalon's Prior Art '855 Patent

15. The asserted claims add nothing inventive or patentable to the disclosures in the prior art. As compared to claim 6 of the '855 patent, the asserted claims recite only the interplanar spacings and 2-theta values intrinsic to Form I armodafinil.

16. Thus, the only question remaining at trial regarding anticipation was: which polymorphic form of armodafinil inherently results from performing Preparation I of the '855 patent? The evidence Defendants presented answered that question unequivocally and without a single contradictory result from Cephalon's experts: a person of ordinary skill in the art (a

"POSA")[1] will necessarily and inevitably obtain Form I armodafinil from following the prior art Preparation I process.

A. Dr. Hollingsworth's Experiments Show That Practicing Preparation I Results in Form I Armodafinil

17. At trial, Defendants' expert Dr. Hollingsworth presented insurmountable evidence that Form I armodafinil is the natural result flowing from Preparation I. He answered the question "What results from Preparation I?" in the most direct way possible: he carried it out, just as a POSA would have done in the late 1990s or early 2000s. Tr. at 123:17-21 (Hollingsworth). He completed two reproductions of Preparation I, and many additional recrystallizations from ethanol, as set out in the '855 patent. Tr. at 91:2-4 (Hollingsworth), 773:5-7 (Myerson).

18. Then, to determine the polymorphic form of the armodafinil he synthesized pursuant to Preparation I of the '855 patent, Dr. Hollingsworth used PXRD analysis—a technique universally recognized as the "gold standard" for determining polymorphic forms. Tr. at 82:5-9, 106:6-7 (Hollingsworth). His PXRD analyses confirmed that his experiments produced Form I armodafinil each and every time. Tr. at 91:9-10 (Hollingsworth).

B. Dr. Hollingsworth Practiced Preparation I as a POSA Would Have Done and Obtained Form I Armodafinil Each and Every Time

19. Preparation I describes a four-step procedure for the synthesis and purification of Form I armodafinil. Tr. at 95:4-6 (Hollingsworth), 717:18-20 (Myerson); JTX-103.3 col. 3, ll. 5-

[1] While the parties' experts offered different views as to the definition of a POSA, Defendants' experts agreed that their opinions were not dependant on which definition the Court adopted. Defendants' experts provided specific testimony regarding that skill level (*see* Tr. at 87:3-18 (Hollingsworth), 384:17-385:5 (Cima)), but their opinions in this matter would remain unchanged if the Court agrees with Cephalon's experts about the definition of a POSA. *See, e.g.*, Tr. at 86:23-88:1 (Hollingsworth); 384:17-385:23 (Cima); 545:23-546:11 (Bernstein).

57. The chemistry involved is straightforward, clean, and uncomplicated. Tr. at 279:9-17 (Lee). Dr. Hollingsworth performed each of the four steps at least twice, and it is undisputed that he did so as a POSA would have done. Tr. at 95:4-6, 96:23-25, 98:24-25, 100:17-101:2, 103:6-7, 123:17-21 (Hollingsworth), 717:18-20 (Myerson).

20. The purpose of step (a) in the overall synthesis is to separate the two enantiomers of modafilic acid by reacting the enantiomers with a complexing agent. Tr. at 95:24-96:5 (Hollingsworth). Dr. Hollingsworth performed step (a)—exactly as it would have been understood and performed by a POSA in the late 1990s or early 2000s—four times. Tr. at 97:1-21 (Hollingsworth); JTX-39.13 *et seq.*, .27 *et seq.*, .43 *et seq.*, .93 *et seq.*

21. The purpose of step (b) is to liberate the R-modafilic acid from the complex created in step (a). Tr. at 100:3-9 (Hollingsworth). Dr. Hollingsworth also performed step (b)—exactly as it would have been understood and performed by a POSA in the late 1990s or early 2000s—four times. Tr. at 98:24-25, 99:6-7 (Hollingsworth); JTX-39.31 *et seq.*, .59 *et seq.*, .85 *et seq.*; JTX-40.35 *et seq.*

22. Step (c) of Preparation I provides for the conversion of the product of step (b) into its methyl ester. Tr. at 110:4-10 (Hollingsworth). Dr. Hollingsworth performed step (c) twice and, like steps (a) and (b), he replicated it as it would have been understood and performed by a POSA. Tr. at 100:17-101:2, 101:14-16 (Hollingsworth); JTX-39.77 *et seq.*; JTX-40.77 *et seq.*

23. The purpose of step (d) of Preparation I is to convert the methyl ester into armodafinil and to purify the resulting armodafinil. Tr. at 101:21-102:1 (Hollingsworth). The last part of step (d) calls for the material to be "recrystallized from ethanol." Tr. at 102:12-14 (Hollingsworth); JTX-103.3, col. 3, ll. 50. Dr. Hollingsworth performed step (d) twice in a manner consistent with the teachings of the '855 patent. Tr. at 103:7; 106:1-2 (Hollingsworth);

JTX-103.3, col. 3: ll. 5-9, 53; JTX-39.107 *et seq.*; JTX-40.91 *et seq.*

24. Through PXRD analysis, Dr. Hollingsworth determined that the crystalline armodafinil he obtained at the end of both Preparation I reproductions was Form I armodafinil. Tr. at 106:6-7, 19, 109:9-12, 110:8-14, 111:5-6 (Hollingsworth), 773:22 (Myerson); DTX-163.6-.7, .13, DTX-255A.5, .389-.390, .448, .459, .596; JTX-40.41, .47; JTX-41.53. He came to this conclusion by comparing the PXRD data he generated for each sample to the characteristic peaks of Form I armodafinil disclosed and claimed in the '570 patent. Tr. at 109:17-21 (Hollingsworth). There is no dispute that the crystalline armodafinil Dr. Hollingsworth obtained in both of his Preparation I replications contained Form I armodafinil. Tr. at 106:19, 109:9-12 (Hollingsworth), 773:22 (Myerson) ("He never failed to get some Form I.").

C. Dr. Hollingsworth Obtained Form I Armodafinil After Additional Recrystallizations of the Product of Preparation I

25. Dr. Hollingsworth did not end his analysis after his two faithful replications of Preparation I. After completing the first synthesis, he performed two additional recrystallizations from ethanol, obtaining Form I armodafinil both times. Tr. at 111:20-21, 112:10-12, 112:22-113:3, 113:10-15 (Hollingsworth); DTX-163.9-.10; DTX-255A.487, .501; JTX-40.57.

26. He also performed an additional ethanol recrystallization after completing the second synthesis. Tr. at 113:21-24 (Hollingsworth). Once more, Dr. Hollingsworth's PXRD work confirmed that the material he obtained was Form I armodafinil. Tr. at 113:19-114:4 (Hollingsworth); DTX-163.16; DTX-255A.6, .380-.382, .625; JTX-41.67.

27. Over the course of his two replications of Preparation I, Dr. Hollingsworth performed five "recrystalliz[ations] from ethanol" and obtained Form I armodafinil each of those five times. Tr. at 114:17-22 (Hollingsworth); DTX-163.6-.7, .9-.10, .13, .16; DTX-255A.5-.6, .380.-382, .389-.390, .448, .459, .487, .501, .596, .625; JTX-40.41, .47, .57; JTX-41.53, .67.

D. Dr. Hollingsworth Obtained Form I Armodafinil Even Before Completing Preparation I

28. Dr. Hollingsworth's work described above demonstrates that Form I armodafinil results when a POSA completes all of Preparation I. His laboratory work also shows that Form I armodafinil naturally flows from following Preparation I even before the end of the process. PXRD testing demonstrates that Dr. Hollingsworth obtained Form I armodafinil after the methanol evaporation part of step (d) in both reproductions of Preparation I. Tr. at 115:15-22, 116:7-14 (Hollingsworth); DTX-163.3, .18; DTX-255A.3, .423-.425, .562-.563; JTX-40.23. PXRD testing and analyses likewise show that he obtained Form I armodafinil after the ether wash part of step (d) in both Preparation I reproductions. Tr. at 116:19-117:17 (Hollingsworth); DTX-163.4, .11; DTX-255A.1, .4, .387-.388, .430-.435, .578-.580; JTX-40.23.

29. Thus, in the course of his two reproductions of Preparation I, Dr. Hollingsworth performed PXRD analysis on ***nine*** samples at various stages in step (d), demonstrating that he obtained Form I armodafinil ***each*** of those ***nine*** times. Tr. at 118:4 (Hollingsworth); DTX-163.3-.4, .6-.7, .9-.10, .11, .13, .16; DTX-255A.1, .3-.6, .380-.382, .387-.390, .423-.425, .430-.435, .448, .459, .487, .501, .562-.564, .578-.580, .596, .625; JTX-40.23, .41, .47, .57; JTX-41.53, .67. Not a single Cephalon witness—nor any cross-examination of Dr. Hollingsworth—challenged Dr. Hollingsworth's conclusion that he obtained Form I armodafinil in each of the experiments he conducted and discussed at trial.

E. Dr. Lee's Experiments Confirm that Practicing Preparation I Results in Form I Armodafinil

30. Dr. Hollingsworth was not the only expert who replicated Preparation I. Defendants also presented the testimony of Dr. Albert Lee, who replicated Preparation I twice and also obtained Form I armodafinil both times.

31. Dr. Lee's laboratory work followed the work performed by Cephalon's experts

Drs. Smith and Selbo, who were instructed to follow Preparation I as they believed a POSA would have—but only up to a point. Tr. at 127:1-13 (Hollingsworth), 277:3-8, 18-21 (Lee). In other words, Cephalon instructed Drs. Smith and Selbo to perform a truncated version of Preparation I. Tr. at 720:11-17 (Selbo). Specifically, step (d) of Preparation I involves three parts: (1) dissolving the substance in methanol and treating with ammonia gas, (2) evaporating the methanol and washing with ether, and (3) recrystallizing from ethanol to obtain crystals. JTX-103.3 col. 3, ll. 43-57.

32. Knowing that Dr. Hollingsworth's experiments showed that Form I inevitably results from a faithful and complete replication of Preparation I, Cephalon specifically instructed Drs. Smith and Selbo to stop their work just before the critical ethanol recrystallization part of step (d). Tr. at 710:22-711:7, 720:10-17 (Selbo). Thus, Drs. Smith and Selbo collectively performed only the first two parts of step (d) even though there were no technical barriers to their completing the ethanol recrystallization step, which they certainly could have done if Cephalon had not instructed them otherwise. Tr. at 721:19-23 (Selbo).

33. Dr. Lee synthesized crystalline armodafinil twice by following the methods used by Drs. Smith and Selbo, including heating to 70-90 °C in step (b) of Preparation I. Tr. at 277:3-8, 283:6-284:14, 286:25-287:3 (Lee); DTX-212. He then finished Preparation I by performing the ethanol recrystallization step as a POSA would have done. Tr. at 286:1-287:3, 10-12 (Lee).

34. Dr. Lee sent his armodafinil samples to Dr. Robie, an expert in PXRD analysis. Tr. at 305:5-6 (Lee). Dr. Robie analyzed the samples and concluded that Dr. Lee made Form I armodafinil each time he replicated Preparation I. Tr. at 345:17-21, 360:6-15 (Robie); Tr. at 305:15-23 (Lee).

35. Dr. Robie drew that conclusion after searching two databases of known crystal

materials for matches to the patterns of the samples he analyzed. Tr. at 353:8-354:13 (Robie). The best match for each sample was Form I armodafinil. Tr. at 354:11-355:3, 355:7-10 (Robie); DTX-339.1-.4; JTX-1.38 at col. 40, ll. 1-8, JTX-89. Thus together, Drs. Lee and Robie's work demonstrates and confirms Dr. Hollingsworth's conclusion, that Form I armodafinil naturally and inevitably results from Preparation I.

F. Cephalon's Experts Performed No Relevant Experiments Leaving Defendants' Results Uncontradicted

36. Tellingly, none of Cephalon's experts performed any complete replications of Preparation I that contradicted the results of Drs. Hollingsworth and Lee. Drs. Myerson and Bernstein did not perform a single experiment. (Tr. at 774:15-20 (Myerson). Drs. Smith and Selbo's experiments and analyses were critically incomplete and flawed because neither expert conducted the required recrystallization from ethanol step. Tr. at 719:2-5, 720:15-17, 720:25-721:10 (Selbo). In particular, Dr. Selbo's PXRD analysis is irrelevant to determining the identity of the ***end*** product of Preparation I. Thus, Cephalon presented no experimental evidence that Form I armodafinil will *not* result from performing a faithful replication of Preparation I from beginning to end.

37. The results and conclusions of Defendants' experts were thus undisputed by all experts who testified about them: in each and every one of the seven ethanol recrystallizations performed by Drs. Hollingsworth and Lee, Form I armodafinil resulted. Tr. at 114:17-22 (Hollingsworth), 305:15-23 (Lee), 773:22 (Myerson).

G. Kofler Hot Bar Analyses Disclosed By The '855 Patent Would Have Produced Form I Armodafinil

38. The record also shows that Form I armodafinil would inevitably result from Preparation I when the melting point analysis disclosed in the '855 patent —which would have been determined by using a Kofler hot bar—is performed. Tr. at 142:16-20 (Hollingsworth)

39. The '855 patent provided a 153-154 °C instantaneous melting point range for the armodafinil produced by Preparation I. JTX-103.3 col. 3, ll. 55. The Kofler hot bar is a metallic strip along which temperature increases from one end to the other. Tr. at 143:2-11 (Hollingsworth). The operator spread the material to be analyzed along the bar, observed where along the bar the material melts, and noted the temperature at that point on the bar. *Id.*

40. Dr. Hollingsworth testified that if, *arguendo,* any form(s) of armodafinil other than Form I resulted from Preparation I, it would necessarily convert to Form I during the instantaneous melting point measurement. Tr. at 143:18-21; 144:2-6, 11-12, 16-20, 144:24-145:3, 145:20-146:1 (Hollingsworth); JTX-1.32 col. 28, ll. 66-67. Cephalon provided data in the '570 patent's file history that demonstrated Forms II and IV converted to Form I at temperatures well within a Kofler hot bar's operating range. Tr. at 143:18-144:12 (Hollingsworth). If those forms were placed on the hot bar, they would necessarily convert to Form I every time the melting point analysis was performed.[2] *Id.*; JTX-38.11-.12.

41. Accordingly, even if Preparation I produced an armodafinil polymorph other than Form I, that polymorph would nonetheless become Form I upon executing the melting point measurement disclosed at the end of Preparation I. Tr. at 145:20-22 (Hollingsworth).

H. Non-Instantaneous Melting Point Data Confirms That Preparation I Results in Form I Armodafinil

42. During prosecution of the '570 patent, Cephalon also provided the PTO with a comparison of the instantaneous melting point listed at the end of Preparation I (153-154 °C), to

[2] Form III is nothing more than a mixture of Forms I and IV, which means it already contains the claimed polymorph. Tr. at 144:16-20 (Hollingsworth). For the same reasons, the Form IV present in the mixture would convert to Form I. *Id.* As for Form V, there is no evidence that this form results from recrystallization from ethanol. Tr. at 144:24-145:3 (Hollingsworth).

the instantaneous melting points it observed with its own Form I armodafinil (156-164 °C). JTX-103.3 col. 3, ll. 55; JTX-38.28-.29, n.7. It relied on the difference in range to argue that the product of Preparation I was not Form I armodafinil. *Id.* Cephalon, however, failed to disclose to the PTO that the Kofler hot bar used to measure instantaneous melting points is an archaic "museum piece." Tr. at 185:16-18 (Hollingsworth), 337:18-21 (Lee). Neither of Defendants' experts used a Kofler hot bar to analyze armodafinil's melting point. Instead, they each used more accurate equipment to measure the non-instantaneous melting points of their samples. Tr. at 185:16-18; 192:12-18 (Hollingsworth), 303:16-18 (Lee); JTX-48.20; *see also* Tr. at 777:18-23 (Myerson).

43. Dr. Hollingsworth's observed non-instantaneous melting points—after the ethanol recrystallization steps from his first reproduction of Preparation I—ranged from 150.4-153.8 °C. Tr. at 139:15-24 (Hollingsworth), 782:5-7 (Myerson); JTX-40.63, .65. These non-instantaneous melting points are the same as Cephalon's data for Form I armodafinil.[3] Tr. at 782:14-783:12 (Myerson); JTX-38.29 at n.7; JTX-40.19, .65, .67; JTX-41.69. The non-instantaneous melting points of the armodafinil Dr. Lee synthesized (150.0-152.8 °C) were also consistent with Cephalon's non-instantaneous melting points for Form I. Tr. at 304:17-21 (Lee).

44. Thus, the most reliable melting point data available—the non-instantaneous measurements—indicates that the crystals that result from following Preparation I are Form I armodafinil. The PTO had none of Drs. Hollingsworth's or Lee's data available when considering whether the '855 patent anticipated the '570 claims. Tr. at 779:2-13 (Myerson).

[3] Cephalon reported that "[t]he [non-instantaneous] melting point obtained for samples of Form I (-)-modafinil ranged between 146.9-157°C, while the melting point of Form II (-)-modafinil ranged between 146-149.6 °C." Tr. at 778:10-13 (Myerson); JTX-38.29, at n.7.

I. Declarations to the PTO During Prosecution of the '570 Patent Support Dr. Hollingsworth's Conclusions

45. Three declarations from Drs. Blomsma, Peterson, and Mallamo submitted to the PTO during the '570 patent's prosecution further support Dr. Hollingsworth's conclusion that Form I naturally and inevitably results from Preparation I. Of the 34 experiments described in these declarations that resulted in crystals, 30 (nearly 90%) unambiguously resulted in Form I armodafinil. Tr. at 130:19-22 (Hollingsworth). The experiments contained in the declarations were not faithful reproductions of Preparation I, and are therefore not directly probative of the anticipation question. But even under conditions that in some instances differed markedly from Preparation I, Form I armodafinil resulted almost all of the time. The four experiments that produced something other than Form I had nothing to do with Preparation I, and therefore provide no useful evidence regarding what crystal form is made by following Preparation I. Tr. at 131:2-7 (Hollingsworth); JTX-38.1-.45. Cephalon's own data therefore demonstrates the ease with which a POSA would have obtained Form I armodafinil by performing Preparation I, even under different conditions. Tr. at 138:21-139:1 (Hollingsworth).

46. Dr. Blomsma admitted that the work done by third party Crystallics and represented in his declaration was not a reproduction of Preparation I. Tr. at 820:8-18 (Blomsma). Instead, the Blomsma declaration sets forth results obtained from a high-throughput polymorph screen. Tr. at 137:12-13 (Hollingsworth), 820:8-18 (Blomsma), 822:25-823:6, 824:15-19 (Blomsma); JTX-38.2. The two experiments described in the Blomsma declaration that resulted in a crystal form other than Form I do not refute that Form I would have necessarily been obtained by a POSA practicing Preparation I. For example, the first experiment was conducted at a scale 4,000 times smaller than that of the scale in Preparation I. Tr. at 137:12-18 (Hollingsworth), 695:24-696:6 (Mallamo); JTX-38.8 (Ex. No. 3). The second experiment used

an exotic cooling rate of 300 °C per minute. Tr. at 137:22-138:10 (Hollingsworth), 692:7-15 (Mallamo); JTX-38.8 (Ex. No. 3). These extreme conditions are not even remotely within the scope of Preparation I.

47. An in-depth analysis of the Peterson declaration reveals similar findings. First, Form I armodafinil resulted in four of the five experiments reported in this declaration, again demonstrating the ease with which it is made. Tr. at 136:9-11 (Hollingsworth); JTX-38.13-.15. The one experiment that resulted in a different polymorphic form was outside the scope of Preparation I because the starting material was spiked with racemic modafinil, a clear departure from Preparation I. Tr. at 136:11-13, 136:18-21 (Hollingsworth); JTX-38.14 at ¶ 7. As a result, this Peterson experiment is not probative of whether Form I necessarily results from Preparation I. Tr. at 137:1-7 (Hollingsworth).

48. The Mallamo declaration discloses similar results. It reports obtaining Form I armodafinil in seven of eight crystallizations, confirming the ease with which Form I is obtained. Tr. at 131:17-18 (Hollingsworth), 695:1-3 (Mallamo); JTX-38.41-.42. The one experiment that resulted in a different form was once again outside of the scope of Preparation I. Tr. at 131:18-20 (Hollingsworth); JTX-38.42. That iteration employed, for example, a rapid cooling rate and a mixture of ethanol with toluene—a solvent that a POSA would not have understood the term "ethanol" to embrace. Tr. at 131:18-132:14 (Hollingsworth); JTX-38.42. Accordingly, this experiment is also not probative of whether Form I necessarily results from Preparation I. Tr. at 132:15-18 (Hollingsworth).

III. A Pharmaceutical Composition Consisting Essentially of Armodafinil's Most Stable Polymorph Would Have Been Obvious to a POSA

49. Defendants also introduced clear and convincing evidence that a POSA would have been motivated to obtain and use Form I armodafinil in a pharmaceutical composition, and

would have had a reasonable expectation of successfully doing so. It was undisputed at trial that Form I is the most thermodynamically stable armodafinil polymorph known. Tr. at 390:4-17 (Cima), 616:11-15 (Bernstein), 840:22-841:11 (Coquerel). That fact, combined with the significant motivation to seek out the most stable form as part of any pharmaceutical development process and the routine nature of obtaining the most stable form, means that it would have taken nothing but routine and predictable steps for a POSA to arrive at the claimed pharmaceutical compositions.

A. A POSA Would Have Been Motivated to Identify Armodafinil's Most Stable Polymorph For Use in a Pharmaceutical Composition

1. Crystalline Armodafinil Was Known to Be Therapeutically Effective

50. First, the therapeutic effectiveness of armodafinil would have been known to a POSA. It is undisputed that the '855 patent expressly discloses the synthesis of crystalline armodafinil and teaches its therapeutic use in pharmaceutical compositions for administration to humans. *Supra* ¶¶ 11-13; JTX-103.1-.5 Abstract, col. 2, ll. 61-66, col. 3, ll. 5-57, col. 6, ll. 44-67, col. 8, ll. 26-29; *see also* Tr. at 381:11-12, 388:7-9, 429:23-430:7 (Cima). The '855 patent specifically discloses that those compositions "consist essentially of" armodafinil. JTX-103.5, claims 2-6; *see also* Tr. at 383:6-9, 425:13-430:8 (Cima), 623:18-20 (Bernstein).

51. Second, because armodafinil was known to be crystalline, a POSA would have known that, like all crystalline compounds, armodafinil has a most stable polymorph. Tr. at 390:21-23, 436:18-21, 437:5-6, 467:16-18 (Cima). The most stable form has the lowest thermodynamic energy. Tr. at 390:6-14 (Cima). Thus, less stable forms naturally tend to transform into the most stable form over time. Tr. at 390:6-20, 453:20-23 (Cima).

2. The Most Stable Polymorph Is the Preferred Form for Pharmaceutical Development

52. By the early 2000s it was well recognized that the most stable polymorph "is by

far and away the preferred in a marketed [drug] formulation." Tr. at 396:5-8 (Cima); s*ee also,* 827:11-16 (Besselievre), 840:22-841:11 (Coquerel), 864:20-865:10 (Rose); JTX-7.2; JTX-104.1 ("Usually, the most stable polymorphic form is preferred in a marketed formulation…"). In fact, Cephalon's expert Dr. Bernstein conceded that the most stable polymorph is often the preferred form and that the use of the most stable form can avoid problems during drug development. Tr. at 617:2-8 (Bernstein).

53. Identification of the most stable polymorph is crucial in drug development because of the significant adverse consequences associated with a change in the polymorphic form during manufacture or storage. JTX-104.1, JTX-21.4; Tr. at 617:2-8 (Bernstein); *see also* Tr. at 396:5-8, 398:10-13, 399:2-5, 453:20-23 (Cima). A POSA would have been well aware that there could be catastrophic commercial consequences for failing to identify the most stable polymorph and instead using a less stable polymorph for drug development. JTX-5.1-.5; Tr. at 395:21-397:15 (Cima); *see also* JTX-104.1 ("Overlooking the most stable polymorph may cause failure of a marketed product due to phrase transformation during storage…").

54. The experience of Abbott Laboratories with the drug ritonavir illustrates why a POSA, or anyone interested in drug development at the time of the alleged invention, would have been motivated to find the most stable polymorph. During development of the drug ritonavir, Abbott failed to confirm that it had the most stable polymorphic form of the API and proceeded to market with less stable form. JTX-5.1; PTX-585.130 at pp. 248-49. After spending hundreds of millions of dollars to develop and market the product, Abbott discovered that the marketed form converted to the most stable form during manufacturing. JTX-104.1; Tr. at 395:21-397:18 (Cima). This forced Abbott to reformulate the product, allowing time for its competitors to take over the market. *Id.* This type of situation, while extremely rare, would have

provided a powerful commercial motivation for a POSA to seek out and use the most stable form of a crystalline active ingredient in a pharmaceutical product as of the time of the alleged invention. Tr. at 397:5-15 (Cima).

55. Accordingly, a POSA would have been highly motivated to identify and use the most stable polymorph of armodafinil in a pharmaceutical composition. Tr. at 381:13-17, 381:25-382:2, 382:22-24, 395:6-9, 442:6-13 (Cima); *see also* JTX-27.4 ("It is essential to ascertain whether the crystalline material… is thermodynamically stable before conducting pivotal trials, since a more stable form may be obtained subsequently, and it may be impossible to produce the metastable form in future synthesis."); Tr. at 827:11-828:6 (Besselievre).

56. Because Form I is the most stable polymorph of armodafinil, the normal and expected desire of a scientist to use the most thermodynamically stable polymorph as the active ingredient in a drug product would have led a POSA directly to armodafinil's most stable polymorphic form (Form I). Tr. at 381:13-17, 381:25-382:2, 382:22-24, 395:6-9 (Cima), 519:13-14, 602:24-605:17, 617:2-8 (Bernstein); JTX-1.19 col. 2, ll. 42-47; JTX-7.2; *see also* Tr. at 390:6-20 (Cima).

B. A POSA Would Have Expected to Obtain the Most Stable Polymorph of Armodafinil Using Well Known and Merely Routine Techniques

57. A POSA would also have had no difficulty obtaining armodafinil's most stable polymorphic form because the most stable polymorph is by far the easiest polymorph to obtain.[4] Tr. at 381:18-24, 411:18-19 (Cima). In light of the '855 patent's disclosures, a POSA would have easily been able to obtain armodafinil's most stable polymorph using nothing more than

[4] This general principle is specifically demonstrated for armodafinil by the recrystallization experiments discussed above. *Infra* ¶ 61, 104-109.

well known and routine techniques, such as ageing or polymorph screening.

1. A POSA Would Have Reasonably Expected to Obtain Armodafinil's Most Stable Polymorph from a Single Ageing Experiment

58. A POSA in the early 2000s would have known that a technique called ageing, also known as solvent-mediated polymorphic transformation, was an efficient method to obtain the most stable polymorph of a crystalline compound. Tr. at 401:16-402:8, 402:13-15, 402:22-403:2 (Cima); JTX-104.1-.2 ("An efficient method to discover the most stable polymorph is the technique of solvent-mediated polymorphic transformation."). Cephalon's expert Dr. Bernstein conceded at trial that slurrying, a type of ageing involving mechanical mixing, is "often used" in industrial crystallizations and "leads to a conversion generally of a mixture of polymorphs to the most stable form." Tr. at 576:24-578:15 (Bernstein).

59. During an ageing experiment, crystals are allowed to remain in contact with a solvent. *See, e.g.,* JTX-27.8. The metastable polymorphs dissolve and recrystallize into a more stable form, continuing until ***only the most thermodynamically stable polymorph*** remains. *See* JTX-104.2 ("The more stable form will then crystallize at the expense of… the less stable form..."); JTX-22.6 ("The cycle continues until only the thermodynamically stable (least soluble) polymorph remains."); JTX-22.7; Tr. at 403:23-404:6 (Cima). Because only the most stable polymorph remains at the end of an ageing experiment, a POSA would have had a reasonable expectation of successfully obtaining armodafinil's most stable polymorph through ageing. Tr. at 404:23-406:13 (Cima). That expectation would have been strengthened by the disclosure in the '855 patent of crystalline armodafinil and ethanol as an appropriate solvent for use in ageing armodafinil. Tr. at 404:14-20 (Cima).

60. In light of the disclosures of the '855 patent, a POSA would have been virtually certain of obtaining armodafinil's most stable polymorph from a single ageing experiment. *Id.*;

see also Tr. at 401:16-403:2, 418:19-22, 456:14-17 (Cima). None of Cephalon's experts testified to the contrary—indeed, Cephalon's expert Dr. Bernstein admitted that "if the manufacturer wants to be sure they get the most stable form, they slurry it… ***in order to make sure that, in the end, the final product is the most stable form.***" Tr. at 577:15-19 (Bernstein) (emphasis added).

61. Further, Cephalon's own documents establish that a POSA would have reasonably expected to obtain Form I armodafinil through an ageing experiment because they show that Cephalon conducted ageing experiments to verify the most stable form of armodafinil and expected those experiments to produce that most stable form. JTX-123.19; PTX-289.2 ("If the polymorphic mixture had converted into only one crystal form, it could be concluded that the 'surviving' form was the more stable (less soluble) form at room temperature. The theory behind this conclusion is that crystals of the more soluble form will dissolve, then recrystallize as the less soluble form… The process will continue until all of the solid phase has converted to the less soluble crystal form.").

62. Cephalon's own ageing experiments confirm that armodafinil's most stable polymorph was easily obtained through ageing. JTX-123.19 ("XRPD was performed… and the powder pattern only showed peaks assigned to Form A.[5] This indicated that Form A was the least soluble and the most stable crystalline form at room temperature."); PTX-289.2; PTX-290.2.

2. A POSA Would Have Reasonably Expected to Obtain Armodafinil's Most Stable Polymorph Through a Conventional Polymorph Screen

63. In the early 2000s, conventional polymorph screening entailed routine steps and common analytical techniques to identify a compound's various polymorphic forms. *See* Tr. at

[5] Cephalon US referred to Form I as Form A. Tr. at 866:18-867:8 (Rose); JTX-64.14.

381:18-19, 416:13-21 (Cima); JTX-21.2, Fig. 1; JTX-25.8, Fig. 3. A POSA would have been able to obtain the most stable polymorph of armodafinil by simple ageing and would not have *needed* to conduct a polymorph screen to obtain Form I armodafinil. Tr. at 418:16-22 (Cima). Nevertheless, a POSA still would have been motivated to conduct a routine polymorph screen on armodafinil and would have reasonably expected to obtain the most stable polymorph of armodafinil during the course of such a screen. Tr. at 406:14-407:13 (Cima).

a. By the Early 2000s Polymorph Screens Were Routine in the Pharmaceutical Industry

64. By the early 2000s, it was widely recognized that most drug compounds exist in multiple polymorphic forms. JTX-22.4, .6; JTX-27.5 ("Those who study polymorphism are rapidly reaching the conclusion that all compounds ... can crystallize in different crystal forms or polymorphs."); JTX-94.7. In fact, polymorphism is so prevalent that Dr. Walter McCrone (acknowledged by Cephalon's expert Dr. Bernstein to be a historically prominent scholar and a giant in the field) concluded that every compound has different polymorphic forms. PTX-28.3; Tr. at 594:11-595:15 (Bernstein); *see also*, JTX-58.19 ("[I]t is clear that probably ***every organic medicinal*** can exist in different polymorphs…") (emphasis added).

65. Although a POSA would have been primarily interested in developing the most stable polymorph as a drug product, he or she would also have appreciated the importance of examining polymorphism. Tr. at 407:11-13, 408:6-14, 411:7-10 (Cima); JTX-21.1, .4; JTX-22.5; JTX-32.2, .9-.10 ("The widespread existence of polymorphic drugs underscores the importance of an efficient and consistent characterization strategy… A thorough understanding of polymorph characteristics also allows selection of the best form to market."); JTX-104.1.

66. Further, FDA published guidelines in 1987 that instructed drug developers to examine polymorphism and stressed the importance of controlling a compound's polymorphic

form. JTX-24.35 ("By the time of an NDA submission, the applicant should have established whether (or not) the drug substance exists in multiple solid-state [polymorphic] forms…"); JTX-21.1; Tr. at 409:5-410:11 (Cima).

67. Thus, by the early 2000s it was routine practice in the pharmaceutical industry to conduct a polymorph screen on drug candidates to both confirm the most stable polymorph and identify additional metastable polymorphs. Tr. at 406:14-407:10, 410:12-23, 416:5-12 (Cima); *see also* JTX-20.5-6; JTX-21.1-.10; JTX-22.5 ("Systematic investigation of a compound to determine whether it is prone to polymorphism . . . is routine practice in pharmaceutical pre-formulation studies.").

b. A POSA Would Have Been Motivated to Conduct a Conventional Polymorphic Screen on Armodafinil

68. A POSA would have expected that armodafinil, like almost every other crystalline drug compound, could exist in multiple polymorphic forms. Tr. at 411:11-16, 412:4-12 (Cima); *see also* JTX-22.6; JTX-27.5. Armodafinil has characteristics associated with polymorphism—such as low solubility in water and a molecular weight below 350. (Tr. at 530:12-22, 592:4-593:8 (Bernstein); JTX-103.3 col. 3, ll. 51-53; PTX-585.127 at p. 242). Thus, a POSA would have been particularly motivated to conduct a polymorph screen on armodafinil. Cephalon's expert Dr. Bernstein agreed that if the armodafinil obtained from Preparation I was a candidate to be an active ingredient in a pharmaceutical composition, there would have been a motivation to perform polymorph screening. Tr. at 618:4-10 (Bernstein).

69. In light of FDA guidelines, the desirability of using the most stable polymorphic form, and the adverse consequences of proceeding to development with a less stable form, a POSA would have been highly motivated to conduct a polymorph screen of armodafinil for both commercial and regulatory reasons. Tr. at 390:11-14, 396:5-8, 406:14-19, 409:5-410: 23 (Cima),

602:24-605:17, 617:2-8 (Bernstein), 827:11-828:6 (Besselievre), 840:22-841:11 (Coquerel), 864:20-865:10 (Rose),; JTX-7.2; JTX-104.1.

c. A POSA Would Have Expected to Obtain Armodafinil's Most Stable Polymorph from Polymorph Screening

70. It would have been a simple and routine matter for a POSA to identify the most stable polymorph of armodafinil from a conventional polymorph screen. Tr. at 406:14-407:10, 416:13-21 (Cima). Because armodafinil was already known to exist in a crystalline form, a POSA would have expected to obtain the most stable polymorph of armodafinil at least 90% of the time from a conventional polymorph screen. Tr. at 381:18-24, 416:22-417:3 (Cima).

71. Moreover, a POSA would have known how to adjust the parameters of a polymorph screen to ensure the formation of armodafinil's most stable polymorph. Tr. at 417:4-14 (Cima). A polymorph screen of armodafinil would have resulted in a limited number of polymorphs. Tr. at 816:17-20 (LeProust). Thus, the evidence conclusively establishes that a POSA would have had more than a reasonable expectation of obtaining armodafinil's most stable polymorph—Form I—through a conventional polymorph screen. Tr. at 411:18-23, 418:3-15, 447:13-21 (Cima); *see also* Tr. at 416:22-417:3 (Cima).

C. The D-Spacings and 2-Theta Values Recited in the Asserted Claims Are Intrinsic to Form I Armodafinil and Would Have Been Measured Using Routine Techniques

72. Upon obtaining armodafinil's most stable form, a POSA would have known to conduct PXRD testing to properly characterize the polymorph. PXRD testing was, and still is, a routine method for identifying and distinguishing different polymorphic crystal forms or polymorphs. Tr. at 82:5-9, 106:3-7 (Hollingsworth), 420:12-23 (Cima), 605:23-606:24, 607:4-22 (Bernstein); *see, e.g.,* JTX-22.28 ("X-ray powder diffraction (XDP) [sic] serves as the primary test for non-equivalence of crystal structures, the XDP pattern of such a species being

unique."). Both Cephalon's and Defendants' experts agree that the actual crystal structure of a polymorph and the PXRD values associated with that crystal structure are inherent characteristics of that polymorph. Tr. at 71:8-73:11 (Hollingsworth), 382:12-18, 421:8-25 (Cima), 607:23-608:5 (Bernstein); *supra* ¶¶ 8-9.

73. Moreover, there is no dispute that the PXRD values recited in the asserted claims are inherent properties of Form I armodafinil. Tr. at 382:12-18, 421:8-21 (Cima); *supra* ¶¶ 8-9. As Cephalon's expert Dr. Bernstein explained, the interplanar spacings "define" and "correspond to a physical dimension in the crystal structure" and the crystal structure is "one and the same" with the claims at issue. Tr. at 505:5-10, 507:2-7, 609:1-4 (Bernstein).

74. Because the d-spacings and 2-theta values specified in the asserted claims are merely inherent properties of Form I armodafinil, a POSA would have been able to identify these values by taking routine PXRD measurements of the most stable polymorph obtained through routine ageing experiments or a conventional polymorph screen. Tr. at 421:18-25, 436:4-9, 436:18-25, 452:8-12 (Cima); Tr. at 607:4-16 (Bernstein); DTX-32.34; JTX-22.28; JTX-37.6 at § 3.3.1(c); JTX-57.8; JTX-94.7. There is no invention in measuring a polymorph's crystal structure using PXRD and reporting the results. Tr. at 382:12-18, 389:1-3 (Cima).

D. A POSA Would Have Been Motivated to Make a Pharmaceutical Composition Consisting Essentially of Form I Armodafinil

75. As described above, a POSA would have been highly motivated to use Form I armodafinil in a pharmaceutical composition. *Supra* ¶¶ 50-56. In view of the '855 patent, a POSA would also have known that crystalline armodafinil could be successfully formulated into an effective pharmaceutical composition for use in humans. Tr. at 383:6-9, 425:13-430:7, 432:8-16 (Cima), 623:18-20 (Bernstein); *supra* ¶¶ 11-13. In light of these express teachings, a POSA would have reasonably expected to successfully formulate Form I into a pharmaceutical

composition. Tr. at 425:8-16, 432:8-16, 433:24-434:7, 460:18-461:3 (Cima).

76. There are extremely rare circumstances where the most stable form of a compound is not sufficiently soluble and instead a metastable or pseudopolymorphic form has been developed as a drug product. Tr. at 461:19-462:17 (Cima). But in light of what is taught by the '855 patent, a POSA would have reasonably expected armodafinil's most stable form to be sufficiently soluble and bioavailable to be effective in a pharmaceutical composition and would not have needed to resort to less stable forms. Tr. at 401:8-15, 425:17-426:15 (Cima).

77. While the '855 patent states that armodafinil is insoluble in water, a POSA would have understood that language to indicate that armodafinil has low solubility in water at neutral pH (and not complete insolubility). Tr. at 427:2-21, 429:1-16 (Cima). That the '855 patent describes the efficacious use of armodafinil pharmaceutical compositions in human clinical trials shows that armodafinil has sufficient solubility and bioavailability when formulated into tablets or capsules. JTX-103.4 col. 6, ll. 44-66; *see also* Tr. at 428:16-20 (Cima); 676:10-18 (Mallamo).

78. Moreover, a POSA would have expected armodafinil's most stable polymorph to be sufficiently soluble and bioavailable for use in a pharmaceutical composition because racemic modafinil, with a lower solubility, was known to be effective in PROVIGIL—Cephalon's earlier commercial drug product. Tr. at 425:13- 426:15 (Cima). Indeed, the '855 patent confirms that armodafinil has "better bioavailability" than racemic modafinil. JTX-103.2.4 col. 1, ll. 60-66, col. 6, ll. 33-37; *see also* Tr. at 427:12-21, 428:2-11 (Cima).

1. If Purification Was Needed, a POSA Would Have Used Routine Techniques

79. While the '855 patent does not expressly discuss the purity of the armodafinil produced by following Preparation I, a POSA would have known how to use routine purification techniques to make that armodafinil suitable for use in a pharmaceutical composition, if

necessary. Tr. at 383:16-21, 430:16-432:16, 458:7-20 (Cima). For example, a POSA would, if needed, have been able to eliminate any polymorphic, chemical, or enantiomeric impurities using routine purification techniques. *Id.*; *see also* JTX-104.2 ("In addition to the preparation of the more stable polymorph, the technique of solvent-mediated transformation [ageing] is also useful . . . to eliminate the less stable polymorph from a polymorphic mixture so as to ensure the phase purity.").

80. Indeed, the fact that the '855 patent does not contain explicit instructions regarding purification or formulation techniques—yet still enables claims to pharmaceutical compositions "*consisting essentially of*" armodafinil—demonstrates the routine nature of the purification process. Tr. at 150:22-151:2 (Hollingsworth); JTX-103.5 col. 7, ll. 18-col. 8, ll. 29.

PROPOSED CONCLUSIONS OF LAW

I. The Differences Between the Prior Art and the Claims at Issue

81. The '855 patent is the closest prior art against the '570 patent claims at issue. Tr. at 386:6-8 (Cima). Because the Preparation I "crystals" disclosed in the '855 patent were Form I armodafinil, and because the remainder of that patent discloses how to make pharmaceutical compositions consisting essentially of armodafinil, no differences exist between the asserted claims and the '855 patent. *Supra* ¶¶ 13, 17-24, 30-35. The claims are therefore anticipated. But even if the Preparation I "crystals" were not Form I armodafinil, the only difference between the claims at issue and the '855 patent would have been the obvious use of the most stable polymorphic form—Form I.

II. The Asserted Claims are Invalid as Anticipated Under 35 U.S.C. §102(b)

82. "To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997). "[A] prior art reference may anticipate without disclosing a feature of the claimed

invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference… [A] limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377, 1379 (Fed. Cir. 2003). If "prior art methods in their *normal and usual operation*" perform the claimed function (or produce the claimed compound), the patent is anticipated. *King Pharms., Inc. v. Eon Labs., Inc.*, 616 F.3d 1267, 1275-76 (Fed. Cir. 2010) (emphasis added).

83. Further, the public has a right to practice the prior art and Cephalon cannot take that right away by claiming the inherent result of following the teachings of the '855 patent. *See Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1348 (Fed. Cir. 1999) ("The public remains free to make, use, or sell prior art compositions or processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate."). There is good reason why the law does not extend patent protection to the discovery of inherent properties in the prior art: allowing such claims would effectively "remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art." *In re Wiseman*, 596 F.2d 1019, 1023 (C.C.P.A. 1979).

84. The evidence presented at trial clearly and convincingly demonstrates that the claimed compositions inevitably result every time a POSA performs Preparation I and practices the '855 patent's teachings to formulate the product of Preparation I into a pharmaceutical composition. *Supra* ¶¶ 15-48.

A. The '855 Patent Expressly Discloses the Subject Matter of the Asserted Claims

85. Asserted claims 6 and 9 must be considered with the limitations of the claims from which they depend, claims 1-4 and 7. Rewritten with these limitations included, the

asserted claims are (JTX-1.38):

> 6. A pharmaceutical composition consisting essentially of a laevorotatory enantiomer of modafinil in a polymorphic form that produces a powder X-ray diffraction spectrum comprising intensity peaks at the interplanar spacings: 8.54, 4.27, 4.02, 3.98, 13.40, 6.34, 5.01, 4.68, 4.62, 4.44, 4.20, 4.15, 3.90, 3.80, 3.43 (Å).
>
> 9. A pharmaceutical composition consisting essentially of a Form I polymorph of (-)-modafinil.

86. While the language in these claims differs, they cover essentially the same thing. As Dr. Hollingsworth explained, the PXRD data incorporated in Claim 6 is that of Form I armodafinil, which is expressly recited in Claim 9. Tr. at 78:23-79:8; 79:23-24 (Hollingsworth); *see also*, Tr. at 388:16-25 (Cima). Broken down, the elements of both asserted claims are: (1) a pharmaceutical composition (2) consisting essentially of (3) Form I armodafinil.

1. The '855 Patent Inherently Discloses Form I Armodafinil

87. As described above, Defendants' experts have demonstrated that Form I armodafinil is the natural and inevitable result of performing Preparation I. Dr. Hollingsworth conducted two complete replications of Preparation I, as a POSA would have done. *Supra* ¶¶ 17-27. Over the course of his two reproductions, Dr. Hollingsworth performed five recrystallizations from ethanol and obtained Form I armodafinil each time. *Id.* Additionally, he demonstrated that Form I armodafinil naturally results from following Preparation I even before the experiment is completed. *Supra* ¶¶ 28-29. Dr. Hollingsworth performed PXRD analysis on nine samples obtained at various stages of step (d), which demonstrated that he obtained Form I armodafinil ***each*** of those nine times. *Id.*; Tr. at 118:4-7 (Hollingsworth).

88. Dr. Lee also performed two complete replications of Preparation I, as a POSA would have. *Supra* ¶¶ 30-35. Dr. Lee followed Dr. Smith's replication of Preparation I (to the point that Dr. Smith stopped), and then completed Preparation I. *Id.* Dr. Robie performed

PXRD testing on Dr. Lee's samples and determined that Dr. Lee made Form I each time. *Id.* The experiments performed by Drs. Hollingsworth, Lee, and Robie demonstrate that practicing Preparation I always results in Form I armodafinil. None of this data was available to the PTO during prosecution of the '570 patent.

89. Cephalon's contention that Defendants' experts "failed to accurately reproduce the '855 Patent," D.I. 300 at 3, has no support in the record. The trial record lacks any evidence suggesting that Defendants' experts departed from Preparation I. In fact, Cephalon's expert Dr. Myerson conceded that Dr. Hollingsworth performed two complete replications of Preparation I, and set forth no criticisms of Dr. Hollingsworth's experimental methods. Tr. at 773:3-7 (Myerson). Dr. Lee's Preparation I reproductions followed the methods of Cephalon's own experts tasked with performing Preparation I as a POSA would have done, albeit a truncated version. *Supra* ¶ 31. The only significant difference between Dr. Lee's work and the work of Cephalon's experts is that Dr. Lee completed Preparation I. *Supra* ¶ 34. The record contains no testimony that Defendants' experts executed anything other than reasonable and accurate replications of Preparation I.

2. The '855 Patent Expressly Discloses Pharmaceutical Compositions Consisting Essentially of Armodafinil

90. Cephalon contends that the Court should construe the asserted claims 6 and 9 as limited to products that contain *only* Form I armodafinil as the active ingredient. D.I. 263 at 10; D.I. 300 at 3. Cephalon bases that contention on the term "[a] pharmaceutical composition consisting essentially of," which this Court construed as: "[a] composition consisting of the specified pharmaceutically active component and optionally unlisted pharmaceutically acceptable ingredients that do not materially affect the basic and novel properties of the specified pharmaceutically active component." D.I. 172 at 2; D.I. 263 at 10; D.I. 300 at 3. In the Court's

construction, "specified pharmaceutically active component" refers to Form I armodafinil. But the language "unlisted pharmaceutically acceptable ingredients" encompasses other ingredients, including armodafinil's other polymorphic forms, insofar as they "do not materially affect the basic and novel properties" of Form I. JTX-3.3; Tr. at 155:7-12 (Hollingsworth).

91. Neither the express language of the asserted claims nor the Court's construction excludes the presence of other polymorphic forms of armodafinil. In fact, the '570 patent states that the invention "relates to the use of" armodafinil Forms II-V "for the manufacture of a medication" and that "pharmaceutical compositions ***according to this invention may also contain another crystalline form of (-)-modafinil*** ... in particular form I and/or another active ingredient ... as a mixture with one or more other polymorphic forms of modafinil such as form II, form III, form IV and form V." JTX-1.24-.25 col. 12, ll. 64-col. 13, ll. 2, col. 13, ll. 9-32 (emphasis added). Thus, the '570 patent teaches that "unlisted pharmaceutically acceptable ingredients" encompasses a mixture of Form I with armodafinil's other polymorphic forms.

92. In view of the express claim language, the '570 patent's specification and the Court's claim construction, a pharmaceutical composition "consisting essentially of" Form I armodafinil according to the invention can include other polymorphic forms of armodafinil. *Supra* ¶ 90-91; *see also* Tr. at 151:3-9, 154:3-11, 155:7-12 (Hollingsworth). Even if the Court were to agree with Cephalon that claims 6 and 9 must contain only Form I armodafinil as the active ingredient, however, the asserted claims are nevertheless invalid because a POSA would have been motivated, and would have known how to purify (polymorphically and/or chemically) the product of Preparation I to meet the "consisting essentially of" limitation. Tr. at 149:15-150:16, 150:22-151:2 (Hollingsworth); 432:8-16, 433:24-434:7 (Cima).

93. To the extent Form I armodafinil has any novelty vis-à-vis the '855 patent, the

interplanar spacings and 2-θ values listed in claims 1-4 constitute its "basic and novel properties." To demonstrate novelty, Cephalon can point to nothing else in the '570 claims that distinguishes them over the '855 patent. The '855 patent expressly discloses crystalline armodafinil and the use of armodafinil in pharmaceutical compositions, and claim 6 of the '855 patent covers a composition "consisting essentially of" armodafinil useful as a central nervous system stimulant. *Supra* ¶¶ 11-13. JTX-103.5 col. 8, ll. 26-29. However, because the claimed interplanar spacings and 2-θ values are intrinsic to Form I armodafinil, another polymorphic form(s) or a chemical impurity would not affect the basic and novel properties of Form I armodafinil. Tr. at 151:3-9, 154:23-155:12 (Hollingsworth).

94. Cephalon asserts that Defendants did not prove anticipation of the asserted claims because Drs. Hollingsworth and Lee failed to identify or quantify the chemical impurities in the Form I armodafinil they synthesized and therefore failed to show suitability for use in a pharmaceutical composition. D.I. 300 at 3. This argument misses the point. Defendants' experts made armodafinil according to Preparation I, and determined that it was Form I. *Supra* ¶¶ 17-24, 31-35. Whether the particular crystals Drs. Hollingsworth and Lee made via Preparation I could be directly formulated into a pharmaceutical composition is irrelevant to the anticipation analysis because the '855 patent ***expressly discloses*** armodafinil produced by Preparation I was used in tablets or capsules in human clinical trials and that it had therapeutic efficacy. *Supra* ¶¶ 11-13; *see also* Tr. at 298:20-23 (Lee). The '855 patent thus discloses Form I armodafinil can be obtained with the purity level necessary for human consumption. *See, e.g., Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991) (recognizing that a single reference may anticipate where the "common knowledge of technologists is not recorded in the reference").

95. Further, the "therapeutic" and "pharmaceutical" compositions claimed in the '855 patent are presumed to be enabled. *See* 35 U.S.C. § 282. Notably, the '855 patent does not describe any purification of armodafinil beyond step (d) of Preparation I. JTX-103.1-.5.[6] Therefore, Form I armodafinil made according to Preparation I is either pharmaceutically acceptable as-is, or techniques to further purify the product of Preparation I were so well-known and routine that they need not be expressly described. *See supra* ¶ 80.

96. Thus, Cephalon's argument that the '855 patent does not anticipate the asserted claims because Defendants purportedly failed to demonstrate the product of Preparation I is suitable for use in a pharmaceutical composition is incorrect.

III. The Evidence Refutes Cephalon's Criticism that Defendants Only Tested a Narrow Scope of Conditions

97. None of Cephalon's critiques of the work Drs. Hollingsworth and Lee performed can save the asserted claims.

A. The Word "Ethanol" in Preparation I Means Absolute Ethanol

98. Cephalon first contends that Defendants' experts did not test Preparation I's full scope because they used only absolute ethanol as the recrystallization solvent. D.I. 300 at 3. However, the evidence shows that "ethanol" in step (d) of Preparation I (which calls for the intermediate product to be "filtered off and recrystallized from ethanol to give CRL 40 982") has only one meaning to a POSA, and that is absolute ethanol. JTX-103.3 col. 3, ll. 50-51; Tr. 133:3-5 (Hollingsworth), 280:22-281:1 (Lee). Further, Cephalon introduced no evidence that a POSA would have interpreted "ethanol" in Preparation I as anything other than absolute ethanol. *See* Tr. at 729:5-11 (Myerson).

[6] The ether wash and recrystallization from ethanol called for in step (d) are purification steps. Tr. at 102:8-10, 125:5-20, 170:3-7 (Hollingsworth); 296:16-19 (Lee); 391:19-392:15 (Cima).

99. Widely accepted industry texts at the relevant time also support Defendants' position. For example, the Handbook of Pharmaceutical Excipients cites to the 1993 British Pharmacopeia which provided that the word "ethanol" without any other qualification refers to absolute ethanol, which is ethanol greater than 99.5 percent by volume. Tr. at 133:17-134:8 (Hollingsworth); JTX-28.3. This handbook further states that "[w]here other strengths are intended, the term 'alcohol' or 'ethanol' is used, followed by the statement of the strength." Tr. at 134:13-15 (Hollingsworth); JTX-28.3. Preparation I of the '855 patent contains no such statement of the strength. Tr. at 134:6-20 (Hollingsworth); JTX-103.3 col. 3, ll. 50.

100. The Merck Index, Tenth Edition, an encyclopedia widely used in the pharmaceutical industry, contains four different definitions for alcohol: "Alcohol, 95%," "Alcohol, Anhydrous," "Alcohol, Denatured," "Alcohol, Diluted." Tr. at 134:23-135:1, 135:7-10 (Hollingsworth); JTX-116.5-.6. Only the definition of "Alcohol, Anhydrous" lists "Ethanol" as a synonym, further supporting Drs. Hollingsworth and Lee's choice of absolute (or anhydrous) ethanol. Tr. at 135:11-14 (Hollingsworth); JTX-116.5.

B. Defendants' Experts Used Reasonable Concentrations and Cooling Rates in the Recrystallization Step of Preparation I

101. Cephalon also argues that Defendants' experts did not test Preparation I's full scope because they used the same armodafinil concentration in the recrystallization step of Preparation I. D.I. 300 at 3. However, the concentration that Drs. Hollingsworth and Lee used was reasonable. Tr. at 169:12-16, 170:1-7 (Hollingsworth), 298:3-17 (Lee).

102. As a POSA would have, Dr. Hollingsworth conducted a small-scale crystallization to determine a suitable concentration of armodafinil for the recrystallization part of step (d). Tr. at 167:1-8 (Hollingsworth), 298:3-17 (Lee); DTX-40.27. He used this suitable concentration throughout his reproductions of Preparation I. Tr. at 167:6-8 (Hollingsworth).

The concentration of armodafinil used by Drs. Hollingsworth and Lee in their respective experiments was reasonable in the context of step (d). Tr. at 169:20-22, 170:1-7 (Hollingsworth), 298:11-17 (Lee).

103. Cephalon further argues that Defendants' experts did not test Preparation I's full scope because they used "slow cooling methods" in the recrystallization part of step (d). But the cooling rates used by Drs. Hollingsworth and Lee in their respective experiments were reasonable, and indeed, standard procedure, considering the purpose of the recrystallization, which is to purify the armodafinil. Tr. at 125:11-19 (Hollingsworth), 296:20-23 (Lee), 393:19-394:15 (Cima) (proper crystallization is slow and selective); JTX-56.3.

C. Cephalon's Own Data Confirms That Form I Armodafinil Results from Most Recrystallization Conditions

104. Cephalon's own data confirms that recrystallizing armodafinil from ethanol would result in the most stable form (Form I) a substantial majority of the time. JTX-14.22; JTX-38.8-.9; JTX-38.13-.14 at ¶¶ 4-5; Tr. at 798:7-799:14 (Peterson); JTX-38.41-.42,; JTX-101.6; JTX-123.19; JTX-125.19; *see* Tr. at 869:20-870:4 (Graf).

105. For example, leaving aside the fact they did not concern reproductions of Preparation I, the declarations submitted during the prosecution of the '570 patent demonstrate that the Form I polymorph is obtained in almost every recrystallization of armodafinil from ethanol. *Supra* ¶¶ 45-48. In fact, the data in the declarations shows that other forms of armodafinil were produced only where extreme conditions inconsistent with the standard recrystallization disclosed in the '855 patent were used. *Id.*

106. Further, in a conventional polymorph screen performed by Cephalon/Lafon around 2000, Form I armodafinil was obtained from a wide variety of recrystallization conditions. Tr. at 845:23-864:4, 852:14-853:18, 854:13-25, 856:6-857:1 (Serrure), 870:25-

871:12 (Neckebrock). In particular, the screen demonstrated that recrystallization of armodafinil from ethanol, even under extreme conditions outside of the '855 patent, almost inevitably results in Form I armodafinil. DTX-51A.6, .9, .17, .20; DTX-51.4, .7; JTX-101.3, .6.

107. A high-throughput screen (not a conventional screen) performed by Crystallics BV in 2003 at Cephalon's request provides further evidence that Form I armodafinil results from a wide range of recrystallization conditions. Tr. at 615:1-11 (Bernstein), 820:13-18 (Blomsma), 861:3-11 (Rose); JTX-38.2 Blomsma Decl. ¶ 3; JTX-62.1. The vast majority of the recrystallization conditions in the screen produced Form I.[7] In fact, Form I was made in 948 out of the 1035 successful recrystallizations conducted.[8] Tr. at 695:17-23 (Mallamo); JTX-14.22; JTX-123.19; JTX-125.19.

108. Based on the results of the Crystallics screen, Cephalon reported to FDA "*more than 95%* of the assigned crystals [were] Form A" and that "scale-up recrystallization studies *only* produced Form A along with an additional solvate." JTX-123.19 (emphasis added); JTX-125.19 (emphasis added); *see* JTX-14.2.

109. Thus, Cephalon's own data shows that nearly any set of conditions that could be described as a "recrystallization" of armodafinil (from ethanol or other solvents) will produce the most stable polymorph—Form I. This data refutes the criticism that Drs. Hollingsworth and Lee tested only a narrow set of recrystallization conditions.

[7] Crystallics (like Cephalon US) used the designation "Form A" for the polymorphic form corresponding to "Form I" in the '570 patent. JTX-38.27 Mallamo Decl. ¶ 16; JTX-64.14.
[8] 177 of the recrystallizations were unsuccessful because the resulting materials could not be identified. JTX-123.19; JTX-125.19.

IV. Cephalon's Speculations Cannot Save the Asserted Claims

A. Cephalon Presented No Evidence That the Product of Preparation I Is Not Form I Armodafinil

110. All of the evidence adduced at trial demonstrates that the product of Preparation I is Form I armodafinil, and that a POSA practicing the prior-art Preparation I process in a normal and usual way obtains Form I armodafinil each and every time. *Supra* ¶¶ 17-48. Tellingly, Cephalon's experts presented no data of their own to rebut Drs. Hollingsworth's and Lee's results. Rather, Cephalon relies only on speculation that Drs. Hollingsworth and Lee deviated so radically from Preparation I that their experiments were no longer representative. D.I. 300 at 3.

111. If performing Preparation I could result in a polymorphic form other than Form I even a ***single*** time, Cephalon would surely have asked its experts to obtain such evidence. There is no dispute that its experts could have performed Preparation I in its entirety. *Supra* ¶¶ 36-37. The problem Cephalon faced, and the clear reason its experts failed to perform a complete replication of Preparation I, is that Preparation I results in Form I every time, as shown by all the record evidence. Cephalon's decision to abstain from any replications of Preparation I is highly suggestive that the natural and necessary product of Preparation I is always Form I armodafinil.

B. Melting Point Data Confirm Preparation I Produces Form I Armodafinil

112. Cephalon suggests Form I armodafinil might not result from Preparation I because the instantaneous melting point reported in the '855 patent does not precisely match what Cephalon believes Form I's melting point should be. Tr. at 700:1-4 (Mallamo). That was the entire basis for Dr. Myerson's unreasonable "expectation" that Form I would not result from Preparation I. Tr. at 774:8-10 (Myerson).

113. The data presented at trial refutes Dr. Myerson's opinion that melting point data in the '855 patent points to something other than Form I. For example, the armodafinil Dr.

Hollingsworth made in his first replication of Preparation I had a non-instantaneous melting point of 150.4-153.8 °C. *Supra* ¶ 43. This falls directly within the 146.9-157 °C non-instantaneous melting point range Cephalon reported to the PTO for Form I. *Id.*

C. Yield Data Confirm Preparation I Produces Form I Armodafinil

114. Cephalon's contention that Drs. Hollingsworth's and Lee's experimental yields are inconsistent with a faithful reproduction of Preparation I also contradicts all available data. The '570 patent, which discusses Preparation I of the '855 patent in detail, explains that the "overall yield" obtained at the end of Preparation I is 5.7%. JTX-1.19 col. 2, ll. 5-13. Drs. Hollingsworth's and Lee's overall yields are very similar to the overall yield of Preparation I as reported in the '570 patent. Tr. at 301:7-12, 343:9-15 (Lee); JTX-40.37; JTX-39.105. Their yield data thus provides further confirmation that Preparation I results in Form I armodafinil.

115. Because the data reported in the '570 patent regarding Preparation I's overall yield supports the conclusions of Drs. Hollingsworth and Lee, Cephalon has attempted to abandon the very yield data its own inventors presented to the PTO. Cephalon now argues the overall yield of Preparation I was 32%, not the 5.7% reported in the '570 specification. Tr. at 686:16-20; 690:7-12 (Mallamo). That argument rings hollow on the record. First, the inclusion in the '570 patent of yield data from the '855 patent was purposeful. The inventors of the '570 patent believed they had a new and useful invention because they had discovered a way to more efficiently synthesize armodafinil compared to Preparation I. Specifically, the '570 patent discloses that the 25% overall yield of the synthesis process described therein is "***markedly greater*** than that obtained in U.S. patent No. 4,927,855." Tr. at 342:14-23 (Lee); JTX-1.25 col. 14, ll. 35-43 (emphasis added).

116. Second, the record shows that Cephalon reviewed the '570 patent for errors, and corrected those errors when necessary—Cephalon filed *two* Certificates of Correction and

provided a *third* correction in the Mallamo declaration. Tr. at 689:9-11 (Mallamo); JTX-1.39-.40; JTX-38.24. None of these corrections mention anything about the allegedly incorrect discussion of yield. Only after Defendants' experts obtained yields closely reflecting the data in the specification of the '570 patent, did Cephalon claim to have suddenly realized that the '570 patent contained at least two additional errors. Tr. at 689:9-14 (Mallamo). Defendants (and the public) must be able to rely on the disclosures of the '570 patent; Cephalon's litigation-inspired disavowals cannot be permitted to trump the teachings (and admissions) of the '570 patent.

117. Finally, Cephalon's self-serving "typo" argument is again nonsensical in view of the record. There is no dispute that Defendants' experts—both unquestionably qualified experts in organic synthesis—replicated Preparation I as a POSA would have. Drs. Hollingsworth's and Lee's yields were close to what the '570 patent inventors understood resulted from following Preparation I. Cephalon's "typo" theory would thus require: (1) that the inventors of the '570 patent grossly misinterpreted the data of their own French colleagues, and (2) the two well-qualified experts everyone agrees replicated Preparation I in fact failed to do so. Neither of those assumptions is supported by the record.

V. The Asserted Claims Are Invalid as Obvious Under 35 U.S.C. § 103

118. Defendants presented clear and convincing evidence of obviousness.[9] A patent may not be obtained if the claimed invention would have been obvious to a person of ordinary skill in the art. 35 U.S.C. § 103(a) (2012). The trier of fact must assess: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the

[9] Defendants presented numerous references at trial not considered by the PTO, including, for example, JTX-24, JTX-32, JTX-57 and JTX-94. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 426 (2007); *Microsoft Corp. v. i4i Ltd. P'ship,*, 131 S. Ct. 2238, 2251 (2011).

claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Obviousness is judged under "an expansive and flexible approach" driven by "common sense." *KSR*, at 415-418. The asserted claims are invalid under this standard.

119. The asserted claims are directed to pharmaceutical compositions consisting essentially of the most thermodynamically stable polymorphic form of armodafinil, Form I. *See supra* ¶¶ 6, 56. The evidence demonstrates clearly and convincingly that a POSA would have been motivated to develop a pharmaceutical composition consisting essentially of Form I armodafinil (*supra* ¶¶ 50-56) and would have been able to do so using no more than routine and well known techniques. *Supra* ¶¶ 57-51. As such, the asserted claims would have been obvious. *See DyStar Textilfarben GmbH v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006) (Obviousness requires consideration of "whether a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and whether there would have been a reasonable expectation of success in doing so.") (citation omitted).

A. The Form I Polymorph of Armodafinil Would Have Been Obvious

120. A POSA clearly would have been motivated to identify armodafinil's most stable polymorph, *i.e.* Form I, because armodafinil was known to have pharmaceutical activity and the most stable polymorph is the preferred polymorphic form to use in a pharmaceutical product. *Supra* ¶¶ 50-56. The unrebutted testimony of Dr. Cima establishes that a POSA would have been virtually certain of obtaining the most stable polymorph of armodafinil by applying well known and routine techniques, such as ageing. *Supra* ¶¶ 57-71.

121. In addition to an ageing experiment, a POSA would have been motivated to conduct a routine polymorphic screen for both commercial and regulatory reasons because failing to use the most stable form could wreak havoc on a marketed product, as illustrated by

ritonavir. *Supra* ¶¶ 53-54. Even Cephalon's own expert Dr. Bernstein admitted that if the armodafinil obtained from Preparation I was a candidate for the active ingredient in a pharmaceutical composition, there would have been a motivation to perform polymorph screening. Tr. at 618:4-10 (Bernstein).

122. The record clearly establishes that a POSA would have been motivated and would have reasonably expected to obtain Form I armodafinil through a routine ageing experiment or a conventional polymorph screen in the ordinary course of drug development. *Supra* ¶¶ 57-71. Indeed, the record shows that armodafinil's most stable polymorph, Form I, is the easiest one to produce. *Supra* ¶ 62; Tr. at 381:5-382:3 (Cima). Because these routine procedures would have produced the most stable polymorph—as a POSA would have expected—Form I armodafinil would have been obvious. *See Merck & Co. v. Biocraft Lab., Inc.*, 874 F.2d 804, 809 (Fed. Cir. 1989) (finding obvious claims that were "[r]eached by means of routine procedures, and producing only predictable results").

123. In sum, the evidence demonstrates that a POSA would have been able to obtain Form I armodafinil through the mere application of known techniques to the teachings of the '855 patent. *See KSR*, 550 U.S. at 417. As such, Form I armodafinil would have been obvious. *Id.* at 417, 421; *see also Brown & Williamson Tobacco Corp. v. Philip Morris, Inc.*, 229 F.3d 1120, 1124 (Fed. Cir. 2000) ("[T]he consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art.") (quoting *In re Dow Chem.*, 837 F.2d 469, 473 (Fed. Cir. 1988)).

124. Another way in which a patent's subject matter can be proved obvious is "by noting that there existed at the time of invention a known problem for which there was an

obvious solution encompassed by the patent's claims." *KSR*, 550 U.S. at 419-20. Assuming *arguendo* that Preparation I results in a less stable polymorph, the "obvious solution" would have been to obtain the most stable form (via a routine ageing experiment or polymorph screen), and then identify its PXRD properties. *Supra* ¶¶ 57-72.

125. When there is a "design need" to solve a problem and there are a limited number of solutions, "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." *KSR*, 550 U.S. at 421. If solving the problem merely required ordinary skill and common sense, the result is not innovative or patent worthy. *See id.* In these circumstances, an obvious-to-try solution renders the claims invalid under § 103. *See id.* In view of the '855 patent, there was a "design need" to determine a suitable polymorphic form of armodafinil for use in a pharmaceutical composition. *Supra* ¶¶ 11-13, 50. Thus, it would have been obvious to try obtaining armodafinil's most stable polymorph (Form I) and to use it in a pharmaceutical composition by merely exercising ordinary skill and common sense.

B. Testing to Obtain Form I Armodafinil Does Not Negate Obviousness

126. That a POSA would have needed to conduct routine testing does not negate the obviousness of the most stable polymorph of armodafinil because that testing was routine in the art. *See Pharmastem Therapeutics Inc., v. Viacell, Inc.*, 491 F.3d 1342, 1364 (Fed. Cir. 2007) ("[s]imply because the formation and properties of a new compound must be verified through testing does not mean that the compound satisfies the test for patentability since the expectation of success need only be reasonable, not absolute") (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1367-69 (Fed. Cir. 2007)). Cephalon's assertion that the prior art gave no indication of what parameters were critical to producing Form I ignores the facts. D.I. 263 at 13.

127. The '855 patent discloses ethanol as an appropriate recrystallization solvent, and Dr. Cima's unrebutted testimony establishes that a POSA would have been able to obtain the

most stable form of armodafinil through simple ageing. *Supra* ¶¶ 58-63, 98. Additionally, a POSA would have been readily able to adjust the recrystallization conditions in a polymorph screen—such as by using a slow cooling rate—to ensure formation of the most stable form. *Supra* ¶ 71. Accordingly, a POSA would have had more than a reasonable expectation of obtaining the most stable form either through ageing or from a polymorph screen.

C. Pharmaceutical Compositions Consisting Essentially of Form I Armodafinil Would Have Been Obvious to a POSA

128. The evidence clearly and convincingly demonstrates that a POSA would have been motivated and able to formulate a pharmaceutical composition consisting essentially of Form I armodafinil—as claimed in the '570 patent—using no more than routine formulation and purification techniques. *Supra* ¶¶ 75-80. Because the '855 patent discloses (i) armodafinil recrystallized from ethanol "in the form of white crystals," (ii) armodafinil's therapeutic advantages when administered in tablets or capsules, and (iii) claims directed to pharmaceutical compositions consisting essentially of armodafinil, this is not a case where the prior art merely teaches a general approach in a promising field of experimentation for a pharmaceutical composition. *Supra* ¶¶ 11-13; Tr. at 619:11-620:10, 623:18-20 (Bernstein). Rather, the prior art directs a POSA toward the asserted claims.

129. Further, a POSA would have reasonably expected that armodafinil's most stable polymorph would work in a pharmaceutical composition because the solubility of modafinil was known through its use in PROVIGIL. Tr. at 425:8-426:15 (Cima); *see also supra* ¶¶ 11-13. Thus, the '855 patent and the testimony of Defendants' experts directly refutes Cephalon's assertion that a POSA "would not have expected that armodafinil would be able to have the seemingly opposed dual properties of being stable enough to use in a pharmaceutical, while remaining soluble enough to provide sufficient bioavailability." D.I. 263 at 14 n.30. Moreover,

other than d-spacing and 2-theta values intrinsic to armodafinil, the asserted claims do not require any particular properties, such as purity, bioavailability, solubility, or stability. JTX-1.38 col. 40, ll. 12-41; Tr. at 430:12-15 (Cima), 610:15-23, 612:17-613:2 (Bernstein). Accordingly, those properties are irrelevant to obviousness of the asserted claims.

130. Due to the known advantages of using the most stable polymorph in a pharmaceutical composition (*supra* ¶¶ 51-56), formulating a pharmaceutical composition consisting essentially of the Form I polymorph of armodafinil is nothing more than a common sense solution to the problem of determining the appropriate solid form of a known active ingredient to use in a drug product. *Supra* ¶¶ 75-80; Tr. at 381:5-383:24, 395:3-9, 396:3-8, 398:8-13, 398:22-399:10, 433:24-434:9 (Cima), 602:24-604:3, 617:2-10 (Bernstein), 827:11-828:6 (Besselievre), 864:20-865:10 (Rose), 840:22-841:11 (Coquerel); JTX-7.2; JTX-104.1. As such, asserted claims 6 and 9 would have been obvious to a POSA. *KSR*, 550 U.S. at 419-21.

D. The D-Spacings and 2-Theta Values Recited In the Asserted Claims Do Not Confer Patentability on the Obvious Use of Form I Armodafinil

131. There is no dispute that the d-spacings and 2-theta values recited in the asserted claims are inherent characteristics of Form I armodafinil. *Supra* ¶¶ 7-9, 72-74. Nonetheless, Cephalon contends that Defendants cannot establish obviousness because there is no prior art suggesting these inherent characteristics. D.I. 300 at 4.

132. Contrary to Cephalon's position, an obvious composition of matter does not become nonobvious by simply measuring an inherent property and claiming the resulting values. *See Santarus, Inc. v. Par Pharm., Inc.*, Nos. 2010-1360, 2010-1380, 2012 WL 3797966, at *9 (Fed. Cir. Sept. 4, 2012). "Just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." *In re Crish*, 393 F.3d 1253, 1258 (Fed. Cir. 2004). "To hold otherwise would allow any

formulation—no matter how obvious—to become patentable merely by testing and claiming an inherent property." *Santarus*, 2012 WL 3797966 at *9.

133. There is no invention in taking a routine PXRD measurement to characterize the crystal structure of a polymorph. Thus, the inherent PXRD characteristics of the most stable polymorph of armodafinil cannot distinguish the asserted claims from the prior art. *See In re Kubin*, 561 F.3d 1351, 1357 (Fed. Cir. 2009); *Atlas Powder*, 190 F.3d at 1347; *cf. In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1351 (Fed. Cir. 2002) (finding anticipation where the patentee "has done nothing more than recognize properties inherent" in prior art compositions).

E. Obviousness Requires Only a Reasonable Expectation of Successfully Obtaining the Claimed Invention

134. It is well settled that "[o]bviousness does not require absolute predictability of success ... *all that is required is a reasonable expectation of success*." *Kubin*, 561 F.3d at 1360 (quotation omitted) (emphasis in original); *see also Merck*, 874 F.2d at 809. Further, "obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." *See Pfizer*, 480 F.3d at 1364. A rule of law equating unpredictability to patentability would mean that any new crystal form would be patentable simply because its intrinsic PXRD properties, such as its d-spacings and 2-theta values, must be determined through testing. *See id.*

135. Nonetheless, Cephalon attempts to insert a "predictability" requirement that is simply not part of the obviousness analysis, arguing that because the exact PXRD properties of polymorphs are unpredictable, Form I armodafinil could not have been obvious. D.I. 300 at 4. In fact, Cephalon's expert Dr. Bernstein erroneously premised his nonobviousness opinion on the belief that "[n]o crystal form can be predicted in advance or known in advance." Tr. at 494:22-495:7, 500:4-10, 546:22-547:3, 571:13-19, 588:8-22 (Bernstein). However, the absolute

predictability of the intrinsic PXRD properties of Form I armodafinil plays no role in the obviousness analysis. *Pfizer,* 480 F.3d at 1364 ("[a] rule of law equating unpredictability to patentability… *cannot* be the proper standard since the expectation of success need only be reasonable, not absolute") (emphasis added). Further, the lack of predictability of conditions for forming ***metastable*** forms is irrelevant to a POSA's expectation of successfully obtaining ***the most stable*** form through a routine ageing experiment or conventional polymorph screen. Tr. at 411:18-23 (Cima); *supra* ¶ 71. For the same reason, Cephalon's reliance on references discussing high-throughput screening techniques is misplaced.

136. Cephalon also wrongly asserts that "[w]hether a person of ordinary skill would expect to obtain the properties of the claimed compound is part of the 'reasonable expectation of success' analysis." D.I. 259 Ex. M ¶ 1172. The reasonable expectation of success concerns making the *claimed invention*, which in this case is a pharmaceutical composition consisting essentially of Form I armodafinil. *Kubin*, 561 F.3d at 1360. The asserted claims specify *only* PXRD values. *Supra* ¶ 129. As discussed above, PXRD properties are intrinsic characteristics of Form I armodafinil that a POSA would have determined with a conventional PXRD analysis, and do not confer patentability on the asserted claims.

137. Cephalon relies on *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1086 (Fed. Cir. 2008), to support the contention that an "obviousness analysis requires a comparison of both the structure and the properties of the claimed inventions with those of the prior art." D.I. 259 Ex. M ¶ 1162. But Cephalon's reliance is misplaced because the court in *Sanofi* considered the properties of the claimed chemical compound in the context of unexpected results. *Sanofi,* 550 F.3d at 1086-90. Here, Cephalon has not alleged that Form I possesses any unexpected

beneficial properties, and unexpected results are not at issue.[10]

138. Further, Form I armodafinil has no advantages over other armodafinil polymorphs. In fact, the '570 patent teaches that armodafinil's *other* polymorphic forms have "advantageous properties in comparison with form I." JTX-1.20 col. 3, ll. 15-17; Tr. at 517:5-14 (Bernstein); 678:17-20 (Mallamo). Neither of the '570 patent inventors (Pierre Leproust and Olivier Neckebrock) offered testimony regarding any purported advantageous properties that were particular to Form I. In fact, when specifically asked to do so, Leproust could not identify any advantageous properties that Form I has compared to armodafinil's other polymorphic forms. Tr. at 817:12-15 (Leproust).

139. Accordingly, the reasonable expectation of success analysis should not include anything beyond what is specified in the asserted claims. To do so would improperly conflate reasonable expectation of success (and thus obviousness) with unexpected results. Here, a POSA would have had motivation and a reasonable expectation of obtaining armodafinil's most stable polymorph using routine techniques, and formulating it into a pharmaceutical composition. Thus ,Form I armodafinil, and pharmaceutical compositions consisting essentially of Form I armodafinil, would have been obvious.

F. Cephalon Relies on Inapposite Case Law

140. To support the assertion that the prior art must teach or suggest the "particular structure" of a claimed polymorphic form to establish obviousness, Cephalon relies on *In re Certain Crystalline Cefadroxil Monohydrate*, Inv. No. 337-TA-293, 15 U.S.P.Q.2d 1263, 1268-69 (I.T.C. Mar. 15, 1990), and *Bristol-Myers Co. v. U.S. Int'l Trade Comm'n*, No. 89-1530, 1989

[10] The Court precluded Cephalon from relying on secondary considerations as sanctions for its discovery violations. (D.I. 225 at 2.)

WL 147230, at *4 (Fed. Cir. Dec. 8, 1989) (nonprecedential). D.I. 259 Ex. M ¶¶ 1165-66. These cases concerned a drug compound produced in 1976, and thus involve a vastly different state of the art and prior art than the '570 patent, which was filed in 2003. *Cefadroxil Monohydrate,* 15 U.S.P.Q.2d at 1267; JTX-1.2.

141. ITC and unpublished Federal Circuit decisions that pre-date the Supreme Court's decision in *KSR* do not control the question of obviousness. As the Federal Circuit has instructed, following *KSR,* courts should "avoid overemphasis on… the explicit content of [prior art references]" because the "sources of information for a properly flexible obviousness inquiry includes… the background knowledge, creativity and common sense of the person of ordinary skill." *Perfect Web Techs., Inc. v. InfoUSA,* 587 F.3d 1324, 1329 (Fed. Cir. 2009) (quoting and citing *KSR,* 550 U.S. 418-21) (affirming obviousness determination even though the prior art did not disclose each claim limitation). For example, in *Kubin,* the Federal Circuit affirmed obviousness, even though the particular sequence of the DNA molecule at issue was not disclosed in the prior art because the prior art generally described the encoded protein, provided a motivation to obtain it, and taught conventional techniques for obtaining the claimed DNA molecule. *Kubin,* 561 F.3d at 1352-55, 1360-61.

142. Here, the prior art discloses crystalline armodafinil, provides a motivation to obtain armodafinil's most stable polymorph, and teaches conventional techniques for obtaining that polymorph. *Supra* ¶¶ 11-13, 50-71. As in *Kubin,* the claims here cover an advance that "would occur in the ordinary course without real innovation." *Kubin,* 561 F.3d at 1361 (citing *KSR*, 550 U.S. at 419). Thus, Defendants need not prove the prior art explicitly disclosed the PXRD characteristics of Form I for obviousness (or anticipation) because they are necessarily present in the most stable polymorph of armodafinil. *See In re Kao,* 639 F.3d 1057, 1070 (Fed.

Cir. 2011) (finding claims obvious in view of a reference that did not expressly disclose a claimed inherent property).

G. Cephalon's Allegations of Hindsight Analysis Are Incorrect

143. Cephalon contends that Dr. Cima based his obviousness analysis on the premise that metastable armodafinil polymorphs were known to exist, and thus improperly relied on hindsight. D.I. 300 at 3-4. Cephalon further contends that the asserted claims would not have been obvious because no prior art taught what the most stable form of armodafinil was likely to be. D.I. 300 at 4. These contentions are meritless. As Dr. Cima explained, regardless of whether multiple metastable polymorphs of armodafinil were known to exist, there is *always* a most thermodynamically stable form of *every* crystalline compound. Tr. at 390:21-23, 436:18-21 (Cima). Therefore, a POSA would have known there was a most stable form of the crystalline armodafinil disclosed in the '855 patent.[11] *Id.*

144. The existence of metastable forms of armodafinil was irrelevant to Dr. Cima's obviousness analysis because it concerned the obviousness of the most stable form of armodafinil, not metastable forms. Thus, Dr. Cima's testimony that metastable forms may be difficult to obtain, but the most stable form of armodafinil would have been easy to obtain, did not demonstrate hindsight. Tr. at 381:18-24 (Cima).

145. Cephalon further contends that the asserted claims would not have been obvious because a more stable form of armodafinil might emerge. D.I. 300 at 4. These arguments lack merit. The '570 patent expressly discloses that the Form I polymorph of armodafinil is the most

[11] The most stable form of armodafinil would have been obvious regardless of nomenclature used—Form I, Form A or Form E. Tr. at 70:15-23 (Hollingsworth), 389:4-14 (Cima); *see also Kao*, 639 F.3d at 1066.

stable form. JTX-1.19 col. 2, ll. 45-47. Cephalon cannot escape that admission now by speculating that it is possible for an even more stable form to be discovered at some indeterminate time in the future.

146. In sum, a POSA would have known that there was a most stable polymorph of armodafinil (*supra* ¶ 51), would have been motivated to use that polymorph in a pharmaceutical composition (*supra* ¶¶ 52-56), would have reasonably expected to obtain that polymorph through routine experimentation (*supra* ¶¶ 57-71), and would have reasonably expected to be successful in formulating a pharmaceutical composition consisting of that polymorph (*supra* ¶¶ 75-80). Accordingly, the asserted claims of the '570 patent would have been obvious.

VI. Conclusion

147. Defendants respectfully request the Court find asserted claims 6 and 9 of the '570 patent invalid under 35 U.S.C. §§ 102(b) and/or 103 in view of the '855 patent in combination with the knowledge of a POSA.

Dated: October 17, 2012

Respectfully submitted,

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DM_US 39310590-2.084848.0018